

Depression as a Predictor for Rehospitalization in Schizophrenia Spectrum Disorders

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Abstract

Purpose: Depression is known to impact the clinical course, outcome and prognosis of Schizophrenia spectrum disorder (SSD), however, this association is still not well established in the literature. We aimed at assessing whether presence of depression and depression with suicidal ideation is associated with rehospitalization in SSD patients.

Methods: A cross-sectional survey of 121 patients with SSD from hospital admission records from 2014 to 2018. Clinical variables associated with rehospitalization in SSD were examined by calculating relative risks (OR) using SAS Logistic regression and Lasso procedure.

Results: Depression in SSD was associated with rehospitalizations. Also, suicidal ideation and depression with suicidal ideation were associated with depression in SSD.

Conclusion: These initial results indicate a need for future studies to explore the extent to which depression and suicidal ideation predicts rehospitalization in SSDs and assess whether dutiful assessment (and treatment) of depression may reduce rates of rehospitalizations among patients with SSDs.

Keywords: Depressive disorder; Schizophrenia spectrum and other psychotic disorders; Hospitalization.

Introduction

Schizophrenia Spectrum Disorders (SSDs) belong to a class of genetically related psychiatric disorders [1-4]. Schizophrenia and schizoaffective disorder are the major types of SSDs [5]. SSDs are debilitating, frequently showing shortened life spans [6]. SSDs can present with positive (hallucinations/delusions) and negative symptoms (anhedonia, avolition, social withdrawal, and apathy). They affect close to 1% of the world's population with an average onset in the early 20s and a male predominance [7]. These disorders are chronic conditions that significantly impact quality of life and even at baseline, a large proportion of SSD patients stay persistently symptomatic with multiple relapses often resulting in long and repeated hospitalizations [8]. The financial burden of these disorders is thus

enormous [9-11]. The World Health Organization report indicates that between 1.6% and 2.6% of the total health costs in western nations is spent on SSD [12]. It has been estimated that anywhere from 15% to 58% of the total direct cost is due to hospitalizations [13,14]. Hospitalization of individuals with SSD has strong correlation with poor clinical outcomes [15-17]. Though prior studies identified exacerbating psychotic symptoms, demographics, personal behaviors, past medical resource usage, and medical comorbidities as predictors for hospitalizations [18,19], there is a dearth of literature on depression as a predictor for hospitalization in SSDs. A previous study reported that depression in SSD is associated with greater number of hospitalizations and that clinical variables associated with depression in SSD were auditory hallucinations, delusions, poor insight and judgment [16].

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Early age of onset, and male gender [18,19] are examples of demographic factors, while low global functioning, psychosocial factor [20,21] reported to be associated with more frequent hospitalizations in the body of literature. Some clinical factors that have been reported in the literature include alcohol use [22], medical non-adherence [23,24], involuntary first admission [25], number of past hospitalizations [26-29], and length of previous hospital stays [20,21]. Other clinical factors associated with increased rates of rehospitalization include exacerbating psychotic symptoms, suicidal ideation, homicidal ideation, and dangerous behaviors as psychiatric symptoms predictive for hospitalizations [30-32]. Another group of predictive factors include psychiatric comorbidities [17]. Depression is a common psychopathological feature among individuals suffering from schizoaffective disorder and schizophrenia [33-36]. Clinically significant depression has also been reported to alter the clinical course of SSDs [16,37,38] and the correlation of depression with suicidal ideation as an indication for hospitalization is well known [30,35].

We therefore hypothesize that depressive symptoms in acutely ill patients with SDD will be associated with increased rehospitalizations and that depressed SSD patients with suicidal ideation will be more predictive of rehospitalizations than depressed SSD patients without suicidal ideation. To test these hypotheses, we calculated the rates of hospitalization for depressed SSD patients with suicidal ideation compared to depressed SSD patients without suicidal ideations and subsequently assessed the association between depression and rehospitalization for SSD.

Methods

This is a cross-sectional survey study made up of a sample of hospital admission records from 2014 to 2018 of Schizophrenia Spectrum Disorders (SSDs) patients according to the Diagnostic Statistical Manual (DSM) IV or DSM V [5,39]. The data collection was based on inclusion criteria approved by the Southern Illinois University School of Medicine Institutional Review Board (IRB). To be eligible, subjects had to have at least one inpatient hospitalization between 2014 and 2018 while patients with comorbid diagnosis of intellectual disability, previously known as mental retardation, were excluded.

Data collection

The variables were operationalized and a database was constructed to serve as the data extraction tool prior to the chart review. All clinical and demographic data were extracted from existing medical records. Data on demographic and clinical variables were obtained from initial hospital admission notes, daily rounding notes, and hospital discharge notes. The chart review was completed between 09/1/2019 to 03/31/2020. Data was collected for multiple admissions where present.

Variables

Our outcome variable for this current study was rehospitalization, a categorical variable. Rehospitalization in this study, is defined as two or more (≥ 2) psychiatric hospitalization versus less than two (< 2) psychiatric hospitalizations. The main predictor variables in this study were depression (present versus absent) and depression with suicidal ideation (depression with suicidal ideation versus depression without suicidal ideation) both categorical variables, while others include demographic factors, race (White versus others), gender (categorical: male versus female), age (continuous), marital status (married ver-

sus single), employment (yes versus no) and health insurance status (present versus absent). All other predictor variables were categorical, including clinical factors: diagnoses, psychiatric symptoms, psychotropic classes, noncompliance and medical comorbidities. Psychiatric diagnoses: schizophrenia versus schizoaffective disorder, psychiatric symptoms (psychosis, Suicidal Ideation (SI) and Homicidal Ideation (HI)) were categorized as present or absent.

Statistical analysis

All data analysis was conducted using SAS software version 9.4 [40]. Frequency distribution and Chi-square test were completed using the PROC FREQ procedure, while means were calculated using the PROC MEANS. The PROC LOGISTIC procedure was used to assess the association between our main outcome variable, rehospitalizations (more than 2 hospitalizations versus less) and predictor variables in separate univariate analyses. We implemented lasso selection to find a parsimonious subset of variables associated with rehospitalization [41]. The variables that were selected by the lasso were subsequently entered into a multivariable logistic regression model. A p-value of 0.05 was required for statistical significance at 95% confidence interval.

Results

The total sample size was 121 patients, with males in the majority (58%). The average age of the sample was 38.1, SD (10.7) years. The patients were mostly unemployed (97%), insured (88%), and single (78%). The detailed demographic features can be found in Table 1.

In univariate logistic regression, depression, suicidal ideation and number of emergency room visits were significantly predictive of rehospitalizations. For more details, see Table 3. All the variables in Table 3 were entered into a lasso selection model. From the lasso selection, comorbidity, suicidal ideation, and ER visits emerged as the selected variables. These variables and depression with suicidal ideation were used to construct final models given our hypothesis. Table 4 summarizes the results of final multivariable models were built using these variables. The first, model include depression with suicidal ideation, comorbidity and ER visits, while the second model were Suicidal Ideation (SI), ER visits and comorbidity. Depression with suicidal ideation and suicidal ideation were strongly associated with increased rehospitalization in models 1 and 2 respectively, while ER visits was only modestly associated with rehospitalization. Comorbidity did not show any association.

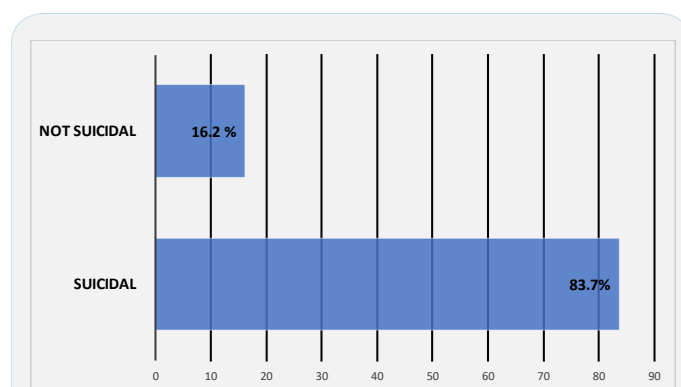


Figure 1: Suicidal ideation in depressed schizophrenia patients

Table 1: Demographic characteristics of study population (n=121).

Variable		Frequency (N)	Proportion (%)
Age Mean (SD)	38.1 (10.7)		
Gender	Male	70	57.9
	Female	51	42.1
Marital status	Single	95	78.5
	Married	7	5.8
	Divorced, widowed or separated (emotional loss)	19	15.7
Insurance status	Insured	3	2.5
	Uninsured	118	97.5
Employment	Yes	14	11.6
	No	107	88.4

Table 2: Descriptive clinical characteristics of sample (n=121).

Variable		Frequency (N)	Proportion (%)
Length of stay [Mean days (SD)]	13.3 (15.1) Range: 1-141		
Number of hospitalizations [Mean (SD)]	1.72(1.41) Range: 1-12		
Number Emergency room visits [Mean (SD)]	1.69 (1.40) Range: 1-12		
Diagnosis	1=Schizophrenia	55	45.5
	2=Schizoaffective disorder	66	54.5
Comorbid diagnosis	1=Yes	33	27.3
	2=No	88	72.7
Non-compliance	1=Yes	23	19.0
	2=No	98	81.0
Psychosis	1=Yes	93	76.9
	2=No	28	23.1
Depression	1=Yes	44	36.4
	2=No	77	63.6
Suicidal ideation	1=Yes	38	31.4
	2=No	83	68.6
Homicidal ideation	1=Yes	19	15.7
	2=No	102	84.3

Discussion

In this present study depression with suicidal ideation and suicidal ideation alone were statistically significantly predictive of rehospitalization in schizophrenia spectrum disorders, even after controlling for effects of other variables. However, potential limitations should be considered before making far reaching conclusions on the results. The sample for this study was limited to a referral teaching hospital in central Illinois and so generalization to the general US population may be a challenge. Another important limitation is the lack of temporal association given the cross-sectional study design.

Table 3: Univariate regression of potential risk factors for rehospitalization (n=121).

Variables	Estimate (Odds ratio)	95% Confidence interval	p-Value
Age	1.00	0.96 -1.05	0.844
Gender	0.63	0.25-1.60	0.331
Race	0.98	0.40-2.44	0.969
Marital status	0.66	0.08-5.75	0.706
Employment	3.56	0.44-28.65	0.233
Length of stay	1.02	0.99-1.05	0.175
ER visits	0.01	0.00-0.007	<0.001
Diagnosis	1.21	0.49-2.99	0.677
Comorbidity	3.13	0.87-11.32	0.081
Non-compliance	1.82	0.49-6.71	0.370
Psychotic symptoms	0.61	0.19-1.96	0.404
Depression	3.51	1.11-11.05	0.032
Suicidal ideation (SI)	3.95	1.10-14.19	0.035
Depression with SI	4.09	1.13-14.79	0.033
Homicidal ideation	0.91	0.27-3.06	0.885

*Significant variables bold.

Table 4: Multivariate regression of potential risk factors of rehospitalization selected using lasso (n=121).

	Variables [†]	Estimate (Odds ratio)	95% Confidence interval	p-Value
Model 1	Depression with SI	5.64	1.13-28.12	0.034
	ER Visits	0.007	0.001-0.060	0.001
	Comorbidity	5.06	0.79-32.37	0.087
Model 2	Suicidal ideation	6.23	1.28-30.40	0.023
	ER Visits	0.006	0.001-0.053	0.001
	Comorbidity	3.56	0.669-18.89	0.137

An odds ratio >1 indicates that the variable is associated with higher likelihood of hospitalization whereas OR<1 suggests lower likelihood of hospitalization.

In this present study, depression was associated with higher rehospitalization rates in univariate analyses consistent with prior studies [16,31]. A possible explanation for this finding is increased risk of harm secondary to depression given the link between suicidal ideation or suicide attempts [31] and psychiatric hospitalization [30,31]. Depressed patients with higher rehospitalizations rates were 80% more likely to have suicidal ideation (see Figure 1). Also, clinically significant depression in the presence of suicidal ideation, has been reported to alter the clinical course of SSDs [16,38,42]. Siris et al ((2001), clearly report significant prevalence of depression in SSDs with approximately 33% patients reporting it in first onset psychotic symptoms during their initial hospitalization, 38% of patients in acute relapse, and 29% of patients with chronic, stable schizophrenia. Rehospitalization due to depression in SSDs is closely interwoven as demonstrated by the study results showing significant odds for rehospitalization for when the depression presents with suicidal ideation compared to depression without suicidal ideation. Therefore, depression is significant in psychosis consistent prior report that depression can serve as a prognosti-

cator in schizophrenia [36]. Considering the evidence, depression is a good candidate for targeted treatment. In addition to having a strong correlation with rehospitalization rates in those with SSD, the available psychopharmacological agents for depression are affordable, effective, and of low-risk [43].

Emergency Room (ER) visits were associated with decreased odds of rehospitalization and persisted in the multivariable model. This finding is counterintuitive, however, given the wide confidence interval it is not robust. Also, known risk factors for hospitalization cluster, and collinearity between the predictor variables in the multivariable model can explain the inconsistent finding [44].

Conclusion

In this initial study, suicidal ideation in those patients with depression significantly predicted rehospitalization for SSD patients. This finding lends support for comprehensive assessment for depression and suicidal ideation in SSD and prompt treatment when diagnoses. However, further well-designed prospective studies using nationally representative sample will be imperative.

References

- Cardno AG, Owen MJ. Genetic relationships between schizophrenia, bipolar disorder, and schizoaffective disorder. *Schizophr Bull.* 2014; 40: 504-515.
- Coryell W, Zimmerman M. The heritability of schizophrenia and schizoaffective disorder. A family study. *Arch Gen Psychiatry.* 1998; 45: 323-327.
- Hodgkinson CA, Goldman D, Jaeger J, et al. Disrupted in schizophrenia 1 (DISC1): Association with schizophrenia, schizoaffective disorder, and bipolar disorder. *Am J Hum Genet.* 2004; 75: 862-872.
- Perkins D, Jeffries C, Jarskog F, et al. microRNA expression in the prefrontal cortex of individuals with schizophrenia and schizoaffective disorder. *Genome Biol.* 2009; 8: 27.
- American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed. Arlington, VA: Psychiatric Publishing. 2013.
- McGrath J, Saha S, Chant D, et al. Schizophrenia: A concise overview of incidence, prevalence, and mortality. *Epidemiol Rev.* 2008; 30: 67-76.
- Hafner H, Maurer K, Loffler W, et al. The epidemiology of early schizophrenia. Influence of age and gender on onset and early course. *Br J Psychiatry.* 1994; 23: 29-38.
- Menezes P, Rodrigues L, Mann A. Predictors of clinical and social outcomes after hospitalization in schizophrenia. *Eur Arch Psychiatry Clin Neurosci.* 1997; 247: 137-145.
- Chapel JM, Ritchey MD, Zhang D, et al. Prevalence and medical costs of chronic diseases among adult Medicaid beneficiaries. *Am J Prev Med.* 2017; 53: S143-S154.
- Cloutier M, Aigbogun MS, Guerin A, et al. The economic burden of schizophrenia in the United States in 2013. *J Clin Psychiatry.* 2016; 77: 764-771.
- Jin H, Mosweu I. The societal cost of schizophrenia: a systematic review. *Pharmacoeconomics.* 2017; 35: 25-42.
- Barbato A. *Schizophrenia and public health*. Geneva: World Health Organization. 1998.
- Rice DP. The economic impact of schizophrenia. *J Clin Psychiatry.* 1999; 60: 4-30.
- Wyatt RJ, Henter I, Leary MC, et al. An economic evaluation of schizophrenia--1991. *Soc Psychiatry Psychiatr Epidemiol.* 1995; 30: 196-205.
- Conley RR, Ascher-Svanum H, Zhu B, et al. The burden of depressive symptoms in the long-term treatment of patients with schizophrenia. *Schizophr Res.* 2007; 90: 186-197.
- Onwuameze OE, Uga A, Paradiso S. Longitudinal assessment of clinical risk factors for depression in schizophrenia spectrum disorders. *Ann Clin Psychiatry.* 2016; 28: 167-174.
- Sands JR, Harrow M. Depression during the longitudinal course of schizophrenia. *Schizophr Bull.* 1999; 25: 157-171.
- Santos A. Factors associated with 30-day readmissions following medical hospitalizations among Medicaid beneficiaries with schizophrenia, bipolar disorder, and major depressive disorder. *Psychiatry Res.* 2020; 291: 113168.
- Hodgson RE, Lewis M, Boardman AP. Prediction of readmission to acute psychiatric units. *Soc Psychiatry Psychiatr Epidemiol.* 2001; 36: 303-309.
- Hendryx M, Russo J, Stenger B, et al. Predicting rehospitalization and outpatient services from administration and outpatient clinical databases. *J Behav Health Serv Res.* 2003; 30: 342-351.
- Suzuki Y, Yasumura S, Fukao A, et al. Associated factors of rehospitalization among schizophrenic patients. *Psychiatry Clin Neurosci.* 2003; 57: 555-561.
- Gerding LB, Labbate LA, Measom MO, et al. Alcohol dependence and hospitalization in schizophrenia. *Schizophr Res.* 1999; 38: 71-75.
- Novick D, Haro JM, Suarez D, et al. Predictors and clinical consequences of non-adherence with antipsychotic medication in the outpatient treatment of schizophrenia. *Psychiatry Res.* 2010; 176: 109-113.
- Sun SX, Liu GG, Christensen DB, et al. Review and analysis of hospitalization costs associated with antipsychotic nonadherence in the treatment of schizophrenia in the United States. *Curr Med Res Opin.* 2007; 23: 2305-2312.
- Fennig S, Rabinowitz J, Fennig S. Involuntary first admissions of patients with schizophrenia as a predictor of future admissions. *Psychiatr Serv.* 1999; 50: 1049-1052.
- Hung YY, Chan HY, Pan YJ. Risk factors for readmission in schizophrenia patients following involuntary admission. *PLoS One.* 2017; 12: e0186768.
- Mojtabi R, Lavelle J, Gibson P, et al. Atypical antipsychotics in first admission schizophrenia: medication continuation and outcomes. *Schizophr Bull.* 2003; 29: 519-530.
- Olfson M, Mechanic D, Boyer C, et al. Assessing clinical predictions of early rehospitalization in schizophrenia. *J Nerv Ment Dis.* 1999; 187: 721-729.
- Perlick D, Rosenheck R, Clarkin JF, et al. Symptoms predicting inpatient service use among patients with bipolar disorder. *Psychiatr Serv.* 1999; 50: 806-812.
- Addington DE, Addington JM. Attempted suicide and depression in schizophrenia. *Acta Psychiatr Scand.* 1992; 85: 288-291.
- Hawton K, Sutton L, Haw C, et al. Schizophrenia and suicide: systematic review of risk factors. *Br J Psychiatry.* 2005; 187: 9-20.

32. Kessler T, Lev-Ran S. The association between comorbid psychiatric diagnoses and hospitalization-related factors among individuals with schizophrenia. *Compr Psychiatry*. 2019; 89: 7-15.
33. Kirkpatrick B, Buchanan RW, Breier A, et al. Depressive symptoms and the deficit syndrome of schizophrenia. *J Nerv Ment Dis*. 1994; 182: 452-455.
34. Huppert JD, Weiss KA, Lim R, et al. Quality of life in schizophrenia: Contributions of anxiety and depression. *Schizophr Res*. 2001; 51: 171-180.
35. Siris SG, Addington D, Azorin JM, et al. Depression in schizophrenia: recognition and management in the USA. *Schizophr Res*. 2001; 47: 185-197.
36. Tollefson G, Anderson S, Tran P. The course of depressive symptoms in predicting relapse in schizophrenia: A double-blind, randomized comparison of Olanzapine and Risperidone. *Biol Psychiatry*. 1999; 46: 365-373.
37. Baynes D, Mulholland C, Cooper SJ, et al. Depressive symptoms in stable chronic schizophrenia: prevalence and relationship to psychopathology and treatment. *Schizophr Res*. 2000; 45: 47-56.
38. Mulholland C, Cooper S. The symptom of depression in schizophrenia and its management. *Adv Psychiatr Treatm*. 2000; 6: 169-177.
39. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, 4th ed, text rev.* Washington, DC: American Psychiatric Publishing. 2000.
40. SAS. SAS version 9.4. SAS Institute. Cary, NC. 2013.
41. Hastie T, Tibshirani R, Wainwright M. *Statistical learning with sparsity. Monographs on statistics and applied probability.* 2015; 143: 143.
42. Thompson E, Neighbors H, Munday C, et al. Length of stay, referral to aftercare, and rehospitalization among psychiatric inpatients. *Psychiatr Serv*. 2003; 54: 1271-1276.
43. Thompson C, Preveler R, Stephenson D, et al. Compliance with antidepressant medication in the treatment of major depressive disorder in primary care: A randomized comparison of fluoxetine and a tricyclic antidepressant. *Am J Psychiatry*. 2000; 157: 338-343.
44. Yoo W, Mayberry R, Bae S, et al. A Study of Effects of MultiCollinearity in the Multivariable Analysis. *Int J Appl Sci Technol*. 2014; 4: 9-19.