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ORIGINAL ARTICLE

Relapse rates and associated factors in patients with schizophrenia: a retrospective study from Brcko District, Bosnia and Herzegovina

Sadina Osmanovic[1], Rusmir Softic[2*], Jasmina Klebic[3], Aida Sehanovic[4]

[1]Department of Psychiatry, Health Centre Brčko District, Brčko, Bosnia and Herzegovina; [2]Department of Psychiatry, University Clinical Centre Tuzla, Tuzla, Bosnia and Herzegovina; [3]Public Health Centre "Dr Mustafa Šehović", Tuzla, Bosnia and Herzegovina; [4]Department of Neurology, University Clinical Centre Tuzla, Bosnia and Herzegovina

ABSTRACT

Aim To determine the proportion of patients with recorded psychiatric rehospitalisation within one year and examine crude associations with antipsychotic treatment patterns and documented medication adherence.
Methods This retrospective cohort study included 87 patients with International Classification of Diseases, 10th Revision schizophrenia (F20.0–F20.9) hospitalised in Brčko District during 2014–2018 and with documented 12-month follow-up. Relapse was defined as recorded psychiatric rehospitalisation due to worsening psychotic symptoms. A separate audit described discharge treatment in 236 hospitalisation records. Exact tests and crude odds ratios (ORs) with 95% confidence intervals (CIs) were calculated.
Results Recorded rehospitalisation occurred in 32/87 patients (36.8%). First-generation antipsychotic exposure (OR 2.11, 95% CI 0.74–6.03; p = 0.215) and antipsychotic polypharmacy (OR 2.16, 95% CI 0.82–5.65; p = 0.164) were not significantly associated with rehospitalisation. Medication non-adherence (OR 11.33, 95% CI 3.58–35.87; p < 0.001) and documented non-cooperation (OR 10.00, 95% CI 3.16–31.62; p < 0.001) showed strong crude associations. In the audit, treatment was identifiable in 183/236 records; polypharmacy was documented in 73.8% and long-acting injectable/depot use in 32.8%.
Conclusion Documented non-adherence and non-cooperation were strongly associated with recorded rehospitalisation. The findings support structured adherence assessment and post-discharge follow-up but do not establish causal effects of antipsychotic class or regimen complexity.

Keywords: antipsychotic agents, medication adherence, patient readmission, polypharmacy, schizophrenia

INTRODUCTION

Schizophrenia is a chronic and disabling psychiatric disorder characterised by disturbances of perception, thought, affect, and behaviour. Relapse prevention is a central therapeutic goal because each relapse may worsen symptoms, reduce psychosocial functioning, increase family burden, and contribute to higher healthcare costs (1–4).

Relapse is commonly operationalised in clinical research as rehospitalisation due to worsening psychotic symptoms, although published definitions vary and may include symptom-scale deterioration, change in treatment, self-harm, suicidality, or violent behaviour (5). Medication non-adherence, substance use, stressful life events, inadequate psychosocial support, and insufficient outpatient follow-up are well-recognised relapse drivers (6,7).

Antipsychotic treatment is the cornerstone of relapse prevention, but routine prescribing may differ substantially from guideline-oriented recommendations. In real-world settings, first-generation antipsychotics (FGAs), second-generation antipsychotics (SGAs), long-acting injectable (depot) preparations (LAIs), and antipsychotic polypharmacy may remain frequent. These patterns are clinically relevant because their interpretation depends not only on drug class but also on indication, adverse-effect burden, adherence, local availability, and continuity of care (8–11).

The novelty of the present study is therefore not the general observation that relapse occurs after discharge or that medication factors are associated with relapse. Its specific added value is the description of relapse and discharge prescribing patterns in a local Southeast European, post-war transitional healthcare setting using routine clinical records. Such data are scarce and may

*Corresponding author:
Rusmir Softic
Department of Psychiatry, University Clinical Centre Tuzla, Tuzla, Bosnia and Herzegovina
E-mail: dr.softic@gmail.com
ORCID ID: 0000-0002-7420-1134

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help clinicians and services identify pragmatic targets for relapse prevention: adherence monitoring, rationalisation of antipsychotic combinations, and clearer documentation of discharge treatment.

The aim of this study was to determine the proportion of patients with recorded psychiatric rehospitalisation within one year after discharge, and to examine its crude association with antipsychotic treatment patterns and documented medication adherence in a real-world psychiatric inpatient cohort.

PATIENTS AND METHODS

Subjects and study design

This retrospective cohort study was conducted at the Psychiatric Department of the Health Centre Brčko District. The source study included patients hospitalised during 2014–2018; data were extracted from medical records and discharge letters using a structured data-collection form.

The patient-level cohort comprised 87 patients with an established International Classification of Diseases, 10th Revision (ICD-10) diagnosis of schizophrenia (F20.0–F20.9) and documented 12-month follow-up in the available medical records. The aggregate database did not permit reconstruction of the total number of records screened before formation of the final cohort. A separate episode-level audit comprised 236 hospitalisation records containing admission or discharge periods, ICD-10 diagnoses, and discharge pharmacotherapy. Because the audit records were organised by hospitalisation episode and lacked verified unique patient identifiers, they were analysed separately and were not linked to patient-level rehospitalisation outcomes.

Methods

Relapse was operationally defined as recorded psychiatric rehospitalisation due to exacerbation of psychotic symptoms within 12 months after discharge. The main patient-level outcome was binary: no recorded rehospitalisation versus recorded rehospitalisation within 12 months. Medication adherence and cooperation with treatment were classified according to documentation in routine clinical records; no standardised instrument was used. The timing of these entries relative to rehospitalisation could not be established consistently, and they were therefore analysed as documented correlates rather than predictors.

First-generation antipsychotic (FGA) exposure was defined as discharge treatment containing at least one FGA, either alone or in combination with a second-generation antipsychotic (SGA). SGA exposure was defined analogously. Descriptive treatment categories were FGA-only, SGA-only, and combined FGA+SGA regimens. Antipsychotic polypharmacy was defined as the simultaneous use of two or more antipsychotic agents. The primary patient-level comparison was monotherapy versus any polypharmacy; regimens containing three or four antipsychotics were reported descriptively in the episode-level audit.

Table 1. Baseline characteristics according to one-year recorded rehospitalisation status

Variable		No rehospitalisation	Rehospitalisation
		N (%)	
Sex	Male	23 (41.8)	7 (21.9)
	Female	32 (58.2)	25 (78.1)
Education	No primary school	4 (7.3)	5 (15.6)
	Primary school	13 (23.6)	8 (25.0)
	Secondary school	24 (43.6)	16 (50.0)
	Higher education	9 (16.4)	1 (3.1)
	University education	4 (7.3)	0 (0.0)
	Unknown	1 (1.8)	2 (6.3)
Marital status	Married	19 (34.5)	15 (46.9)
	Single	18 (32.7)	3 (9.4)
	Divorced	13 (23.6)	7 (21.9)
	Widowed	5 (9.1)	7 (21.9)

Table 2. Treatment-related variables and one-year recorded rehospitalisation

Variable		No rehospitalisation	Rehospitalisation	Crude OR (95% CI)	p
		N (%)			
FGA exposure	Yes	37 (67.3)	26 (81.2)	2.11 (0.74–6.03)	0.215
	No	18 (32.7)	6 (18.8)	—	
Antipsychotic polypharmacy	Yes	32 (58.2)	24 (75.0)	2.16 (0.82–5.65)	0.164
	No	23 (41.8)	8 (25.0)	—	
Number of antipsychotics	One	23 (41.8)	8 (25.0)	—	0.136
	Two	29 (52.7)	19 (59.4)	—	
	Three	3 (5.5)	5 (15.6)	—	
Medication non-adherence	No regular medication use	5 (9.1)	17 (53.1)	11.33 (3.58–35.87)	< 0.001
	Regular medication use	50 (90.9)	15 (46.9)	—	
Medication non-cooperation	Non-cooperative	5 (9.1)	16 (50.0)	10.00 (3.16–31.62)	< 0.001
	Cooperative	50 (90.9)	16 (50.0)	—	

CI, confidence interval; FGA, first-generation antipsychotic; OR, odds ratio. Fisher's exact test was used for 2×2 comparisons and the Fisher-Freeman-Halton exact test for the three-category comparison. ORs are crude; em dashes indicate reference categories.

Discharge pharmacotherapy was reviewed to identify individual antipsychotics, antipsychotic class, and long-acting injectable/depot use. The available records included haloperidol, chlorpromazine, fluphenazine, promazine, levomepromazine, clozapine, risperidone, sulpiride, aripiprazole, and olanzapine. Concomitant non-antipsychotic drugs were not counted as antipsychotic polypharmacy. Antipsychotic treatment was identifiable in 183/236 audit records; drug-specific analyses were restricted to these records, and no imputation was performed for the remaining 53 records.

Statistical analysis

Categorical variables are presented as n (%), and age as median. Fisher's exact test was used for 2×2 comparisons and the Fisher–Freeman–Halton exact test for larger contingency tables. Crude odds ratios (ORs) with 95% confidence intervals (CIs) were calculated from the available aggregate 2×2 tables. Because complete individual-level data were unavailable, multivariable logistic regression was not performed. Two-sided p values < 0.05 were considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA), and exact contingency-table calculations were verified from the displayed aggregate counts.

RESULTS

The patient-level cohort included 87 patients. The median age was 43 years. Women comprised 57/87 (65.5%) and men 30/87 (34.5%) of the cohort. Recorded psychiatric rehospitalisation within one year occurred in 32/87 patients (36.8%), while 55/87 (63.2%) had no recorded rehospitalisation in the available medical records (Table 1).

FGA exposure was documented in 26/32 patients with recorded rehospitalisation (81.2%) and 37/55 without recorded rehospitalisation (67.3%) (OR 2.11, 95% CI 0.74–6.03; p = 0.215). Antipsychotic polypharmacy was observed in 24/32 (75.0%) and 32/55 (58.2%) patients, respectively (OR 2.16, 95% CI 0.82–5.65; p = 0.164). Neither association was statistically significant. Medication non-adherence was documented in 17/32 patients with recorded rehospitalisation (53.1%) and 5/55 without recorded rehospitalisation (9.1%) (OR 11.33, 95% CI 3.58–35.87; p < 0.001). Documented non-cooperation with treatment was present in 16/32 (50.0%) and 5/55 (9.1%) patients, respectively (OR 10.00, 95% CI 3.16–31.62; p < 0.001) (Table 2).

Discharge antipsychotic treatment was identifiable in 183/236 hospitalisation records (77.5%); 53 records (22.5%) were excluded from drug-specific analyses because treatment could not be identified. The most frequently documented antipsychotics were promazine in 89/183 records (48.6%), haloperidol in 73/183 (39.9%), clozapine in 59/183 (32.2%), fluphenazine in 55/183 (30.1%), and chlorpromazine in 31/183 (16.9%). Levomepromazine was recorded in 12/183 records (6.6%), risperidone in 5/183 (2.7%), sulpiride in 4/183 (2.2%), and aripiprazole and olanzapine in 3/183 records each (1.6%) (Table 3).

Among the 183 hospitalisation records with identifiable discharge antipsychotic treatment, FGA-only regimens were documented in 113 records (61.7%), SGA-only regimens in 20 (10.9%), and combined FGA+SGA therapy in 50 (27.3%). At least one FGA was recorded in 163/183 records (89.1%) and at least one SGA in 70/183 (38.3%). Monotherapy was documented in 48 records (26.2%), whereas polypharmacy was present in 135 (73.8%), including two antipsychotics in 120 (65.6%), three in 14 (7.7%), and four in one record (0.5%). Long-acting injectable/depot antipsychotics were documented in 60/183 records (32.8%) (Table 4).

Table 3. Antipsychotics identified in discharge treatment records

Antipsychotic	N (%)
Promazine	89 (48.6)
Haloperidol	73 (39.9)
Clozapine	59 (32.2)
Fluphenazine	55 (30.1)
Chlorpromazine	31 (16.9)
Levomepromazine	12 (6.6)
Risperidone	5 (2.7)
Sulpiride	4 (2.2)
Aripiprazole	3 (1.6)
Olanzapine	3 (1.6)

Denominator: 183 hospitalisation records with identifiable discharge antipsychotic treatment.

Table 4. Antipsychotic treatment patterns in discharge treatment records

Treatment pattern	n (%)
Regimen by antipsychotic class	
FGA-only regimen	113 (61.7)
SGA-only regimen	20 (10.9)
Combined FGA+SGA regimen	50 (27.3)
Any FGA exposure	163 (89.1)
Any SGA exposure	70 (38.3)
Number of antipsychotics	
Monotherapy	48 (26.2)
Any antipsychotic polypharmacy	135 (73.8)
Two antipsychotics	120 (65.6)
Three antipsychotics	14 (7.7)
Four antipsychotics	1 (0.5)
Long-acting treatment	
LAI/depot antipsychotic documented	60 (32.8)

Denominator: 183 hospitalisation records with identifiable discharge antipsychotic treatment. Records with unidentifiable treatment (n = 53) were excluded from drug-specific analyses.
FGA, first-generation antipsychotic; LAI, long-acting injectable; SGA, second-generation antipsychotic.

DISCUSSION

Recorded psychiatric rehospitalisation within one year occurred in 36.8% of this cohort. The clearest crude associations were with documented medication non-adherence and non-cooperation, whereas FGA exposure and antipsychotic polypharmacy were not significantly associated with rehospitalisation. Because the timing of adherence documentation could not be established consistently, these findings should be interpreted as clinical correlates rather than independent predictors.

The association with non-adherence is consistent with evidence that irregular medication use contributes to symptom recurrence and rehospitalisation (5–8). In routine care, non-adherence and non-cooperation are likely to overlap and may reflect limited insight, adverse effects, dissatisfaction with treatment, insufficient family support, or discontinuity of care. Their documentation should therefore prompt early review of barriers

to treatment rather than being treated as two separate mechanisms.

The higher frequency of FGA exposure and polypharmacy among patients with recorded rehospitalisation should be interpreted cautiously. Maintenance antipsychotic treatment reduces relapse risk (9), but patients with more severe illness, previous treatment failures, or adherence difficulties are also more likely to receive long-acting preparations or several antipsychotics. This confounding by indication complicates comparisons between regimens. Reviews have reported heterogeneous findings on antipsychotic polypharmacy (10–12), while a large observational study found that some combinations were associated with lower rehospitalisation than monotherapy (13).

The episode-level audit showed frequent use of FGAs, antipsychotic combinations, and long-acting injectable/depot preparations in this service. These patterns may reflect local availability, previous treatment response, established prescribing practice, and attempts to address adherence difficulties. Because the audit was organised by hospitalisation episode rather than verified individual patient, it could not link a discharge regimen to subsequent rehospitalisation. In addition, treatment was not identifiable in 22.5% of audit records and dose documentation was insufficient for standardised dose comparisons.

Clinical course may also be influenced by factors not examined in this study, including illness severity, substance use, psychosocial circumstances, symptom profile, and the biological heterogeneity of schizophrenia (14).

Several limitations should be considered. The study was retrospective and single-centre, the total number of records screened before formation of the 87-patient cohort could not be reconstructed, and rehospitalisations outside the available records may have been missed. Complete individual-level data were unavailable, precluding multivariable adjustment, and the timing of adherence and cooperation documentation relative to rehospitalisation was uncertain. Substance use, psychopathology severity, psychosocial functioning, family support, adverse effects, and intensity of outpatient follow-up were not consistently recorded. The results therefore support structured adherence assessment, early post-discharge follow-up, family involvement where appropriate, and individual review of complex regimens, but they do not establish causal effects.

CONCLUSION

Recorded psychiatric rehospitalisation within one year occurred in 36.8% of patients. Documented non-adherence and non-cooperation showed strong crude associations with rehospitalisation, whereas FGA exposure and antipsychotic polypharmacy were not significantly associated. The separate episode-level audit showed frequent use of FGAs, antipsychotic combinations, and long-acting injectable/depot preparations. These findings support structured adherence assessment and post-discharge follow-up, with individual review of complex antipsychotic regimens when clinically appropriate.

FUNDING

No specific funding was received for this study.

CONFLICTS OF INTEREST

None to declare.

ETHICS STATEMENT

The study was approved by the Ethics Committee of Health Centre Brčko (approval No. 05-003/19-1; 15 April 2019). Because of the retrospective design and use of de-identified routinely collected medical data, the requirement for individual informed consent was waived.

DATA AVAILABILITY STATEMENT

The aggregate patient-level tables and the de-identified episode-level pharmacotherapy dataset used in this analysis are available from the corresponding author on reasonable request, subject to institutional and ethical approval.

AUTHOR CONTRIBUTIONS (CRediT)

Conceptualization: S.O., R.S.; **Formal analysis:** S.O., R.S.; **Methodology:** S.O., R.S., J.K.; **Supervision:** R.S.; **Writing – original draft:** S.O., R.S., J.K.; **Writing – review & editing:** S.O., R.S., J.K., A.S. All authors have read and agreed to the published version of the manuscript.

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