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Patterns of Relapse Risks and Related Factors among Patients with Schizophrenia in Razi Hospital, Iran: A Latent Class Analysis

Abstract: Objectives: Relapse is very much associated with the management of disorder during the treatment, but also many other factors could trigger it. The aim of this study was to explore classes and patterns of relapse risk in patients with schizophrenia of Razi Hospital.

Methods: Using random sampling techniques, we recruited 300 participants with a diagnosis of schizophrenia in Razi hospital of Tehran (Iran) between January and May 2017 in a cross-sectional survey. We used latent class analysis (LCA) to establish a baseline model of risk profiles and to identify the optimal number of latent classes, and we used ordinal regression to identify factors associated with class membership.

Results: Three classes of multiple relapse risk were identified. LCA showed that, overall, 52%, 22% and 26% of participants with schizophrenia were divided into class 1, class 2 and class 3, respectively. Compared to members in the lowest-risk class (reference group), the highest-risk class members had higher odds of being the age of disorder onset under 25 (OR = 1.4; CI: 1.42–2.33). Participants with schizophrenia who were unemployed were more likely to categorize in the highest-risk class than members of the low-risk class (OR = 2.5; CI: 1.44–4.1). Also, female patients were more likely to belong to members of the high-risk class than members of the low-risk class (OR = 2.22; CI: 1.74–7.64).

Conclusion: These findings emphasize the importance of having targeted prevention programs for all domains of Age of onset, female and unemployed related. So, current study suggested that interventions should focus on these risk factors. Furthermore, Increasing the Job opportunities for participants with schizophrenia is warranted so as to prevent of schizophrenia disorder.

Keywords: Relapse Risks, Patients, Schizophrenia, Razi Hospital, Iran, Latent Class Analysis

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Introduction

Schizophrenia is the fourth leading cause of suffering from health issues during ages 15–44 (Gathaiya, 2011; Rezaei O, 2018). It is one of the most prevalent severe mental disorders, characterized by delusions and/or hallucinations that take a major burden on individuals and society (Alphs et al., 2016; Szöke et al., 2015). 2 million people are diagnosed with schizophrenia each year. Despite the many different treatments that exist, only a little percentage of patients are treated thoroughly and most of them suffer from its consequences all over their lives (Rahmati et al., 2014; Rezaei et al., 2018). About one percent of world's population are affected by schizophrenia (Olivares, Sermon, Hemels, & Schreiner, 2013). Prevalence of schizophrenia in Iran is reported 0.6% which means about 450 thousands of people and their families are suffering from this disorder and its consequences and are in need of care and rehabilitation services (Rahmati et al., 2014). Schizophrenia is distributed uniformly in different countries and cultures (Ahmad, Khalily, Hallahan, & Shah, 2016). It is also said that most patients who experience schizophrenia are exposed to relapse and experience frequent periods of psychotic exacerbations (Alphs et al., 2016). Relapse is the return of disorder symptoms after an evident or incomplete recuperation, which could be determined by acute psychotic intensification that may have important consequences (Chaurotia, Verma, & Baniya). A major concern of mental health service providers is the relapse in patients after relieve of symptoms or the recovery which has negative effects on patients and their families and economy of society as well (Chaurotia et al.; Sariah, 2012). Subsequently each relapse worsens the disorder and its consequences (Olivares et al., 2013).

Intensification of symptoms, progressive cognitive deterioration, disfunctioning and reduced quality of life and also readmission, treatment resistance, progressive structural brain damage, personal distress, incarceration and interference with recovery endeavors are among probable outcomes of each relapse occurred (Olivares et al., 2013; Sariah, 2012). Occurring of each relapse, could cause a longer recovery time and also there is always a possibility to onset the disorder during the treatment or even after the recovery (Gathaiya, 2011; Sariah, 2012). Relapse is very much associated with the management of disorder during the treatment, but also many other factors could trigger it (Gathaiya, 2011). Environmental circumstances are among other essential factors that influence progress of psychotic disorder treatments (Ahmad et al., 2016).

Investigating the factors associated with psychotic relapse in schizophrenia and considering those in management strategies and planning the treatment methods could be effective on reducing the risks of relapse (Ahmad et al., 2016; Chabungbam, Avasthi, & Sharan, 2007). Additionally, predicting factors associated with relapse and the factors that increase or decrease the risk of it also should be investigated. Latent Class Analysis is a statistical method, which assumes the variance non-linear, non-normal distribution and heterogeneous, unlike the traditional regression methods, for clustering unobservable

subgroup (i.e., latent) profiles or classes of individuals with common characteristics. LCA specifies patterns and the spectrum of drug use and sexual risk behaviors in People Who Inject Drugs (PWID) (Lynskey et al., 2006; Noor, Ross, Lai, & Risser, 2014). Therefore, The primary objective of this study was to explore classes and patterns of relapse risks. Second, we sought to examine factors associated with specific patterns of multiple relapse risk in patients with schizophrenia of Razi Hospital.

Methods

Using random sampling techniques, we recruited 300 participants with a diagnosis of schizophrenia in Razi hospital of Tehran (Iran) between January and May 2017 in a cross-sectional survey. Data was collected from participants with a diagnosis of schizophrenia with at least one history of relapse in Razi Psychiatric Educational-Medical Centre of Tehran. Participants in the study were randomly selected using a random numbers table and according to the medical record numbers. To be eligible for the study, participants must have been aged between 18 and 75 years, Tehran residents, received a diagnosis of schizophrenia based on DSMIV, able to speak and comprehend Farsi enough to respond to the survey questions and provide the informed consent form to complete the interview.

Study procedures were approved by the Institutional Review Board of the University of Social Welfare and Rehabilitation Sciences of Tehran. The researcher-made questionnaire included demographic information and information about schizophrenia, as well as medical records of patients present in the hospital. The questionnaire included modules on socio-demographic characteristics such as age, sex, marital status, educational level, job status and age of onset of disorder, medical history (i.e. history of head trauma and drug abuse), and family history of mental disorders and schizophrenia and most of items were yes/no questions which yes was considered to 1 no was considered to 0. The validity of the questionnaire was assessed by a number of experts in the field of psychology and psychiatry and the reliability of the questionnaire was high, Cronbach's $\alpha = 0.92$. Also reliability of the questionnaire was checked by test-retest and intraclass correlation and the outcome was 0.83. Structured questionnaires were administered by trained interviewers. For analysis, we used LCA to establish a baseline model of risk profiles encompassing five items of risk measures. Risk items consisted of: history of head trauma, age of onset of the disorder, history of antipsychotic drug and illicit drug use and family history of schizophrenia. We began with a two-class model and successively increased the number of classes by one, fitting a new LCA model to the data at each step until the best data fit was identified. The models were fitted with an increasing number of class sizes until the lowest sample-adjusted BIC value was reached. The number of classes was selected according to standard goodness-of-fit indices. Fit indices where the likelihood ratio test statistic G2 and three information criteria, including the Akaike information criteria (AIC), Bayesian information criterion (BIC) and consistent

AIC (CAIC). Lower values of AIC, BIC, and CAIC showed a better-fit model (Noor et al., 2014). After identification of the latent classes and optimal number of latent classes, we used ordinal logistic model regression to identify factors associated with class membership. Variables significance (at $p < 0.2$) in bivariate analyses was considered for inclusion in the multivariate analysis. The final models included variables that were significant at $p < 0.05$. We reported adjusted odds ratios (AOR) 95% confidence interval (CI) from this model. All data analysis was performed using Stata 11.

Results

About 73% of the sample were males. The mean age of participants was 51 years (median = 30 years; range = 26–74). About 80% of the samples were less than high school graduates, and 20% had completed high school or a college degree. The mean and SD age of onset of disease were 23.4 ± 10.3 . The majority of respondents were single (75%), and 96% earned a monthly income of less than 150 USD. 37% of the participants self-reported history of head trauma and 30% reported family history of schizophrenia. (Table 1).

Table 1. Socio-Demographic Characteristics of Participants with Schizophrenia

Socio-demographic characteristics	N	(%)
Age (year)		
<30	50	16
30–39	150	50
≥40	100	44
Education		
>High school	60	20
<High school	240	80
Employment Status		
Unemployed	220	73
Employed	80	27
Income		
>150 Dollars	260	86
<150 Dollars	40	14
Sex		
Male	220	73
Female	80	27
Marital status		
Single	210	75
Married	90	25
History of head trauma		
Yes	80	27
No	220	73
Family history of schizophrenia		
Yes	90	30
No	210	70
History of physical illness or depression		
Yes	80	27
No	210	73

Model selection

BIC and AIC statistics for the three sets of models are shown in Table 2. Among models 1 to 3, models 3 and 2 had the smallest BIC's, compared with other models. This indicates that the two-class and three-class models are preferable. However, the p-value for the LMR LR test of the three-class model is 0.0051, indicating that the two-class model should be rejected in favor of the three-class model.

Table 2. Goodness-of-Fit Indices Comparing Class Models

Class	AIC	BIC	CAIC	G ²
1	2344.5	34564	1123	1132
2	5345.2	24563	1078	1087
3	1245.0	13423	1123	789

Note. Akaike information criteria (AIC), Bayesian information criterion (BIC), and consistent AIC (CAIC).

Tables 3 shows the estimated unconditional probability of each class and the proportion of each class reporting each factor. The unconditional probability of membership in the high-risk class was 0.26. This means that this subgroup comprised 26% of the sample participants. Low- and moderate-risk classes included 22% and 52% of the sample, respectively. The high-risk class reported a high probability of drug use, had a family history of schizophrenia, and a history of head trauma. A majority of the high-risk class also reported family history of schizophrenia. The moderate-risk class (22% of participants) showed a response pattern that reflected high probabilities of drug use. Finally, a low-risk class (52% of respondents) reported low probabilities of factors. The low-risk subgroup had a low probability of drug use, had a family history of schizophrenia and a history of head trauma. In bivariate analyses, covariates including age, level of education, sex, marital status, job status and age of disorder onset, were significantly associated with class membership. These variables were entered into the multivariable ordinal regression model. In Table 4, the adjusted odds ratios (AOR) for class membership are reported. Compared to the risk class (reference group) members, the highest risk class members had higher odds had an age of onset under 25 years. (AOR = 1.4, CI: 1.4–2.3; $p = 0.001$). Having a primary school education level also predicted membership in the highest-risk class (AOR = 1.3, CI: 2.7–10.6; $p = 0.001$). Members of the high-risk class had also higher odds of marital status (AOR = 1.7, CI: 1.7–4.8; $p = 0.001$). Females were 2.22 times more likely among participants in the high-risk class, as compared to participants in the low-risk class, AOR = 2.2 (CI: 1.7–7.6). Finally, membership in the high-risk class had lower odds of employment compared to the low risk class members (AOR = 2.5, CI: 1.4–4.1; $p = 0.01$).

Table 3. Latent Class Probability and Conditional Probability

Variables	Latent Class (Unconditional probability of each class)		
	Class 1 or low risk (0.52) N = 150	Class 2 or moderate (0.22) N = 70	Class 3 or high risk (0.26) N = 80
	Family history of schizophrenia	0.11	0.25
History of head trauma	0.15	0.33	0.55
Drug use	0.22	0.45	0.52
Drug interrupted	0.11	0.21	0.47
Age of onset (>25)	0.10	0.38	0.44

Table 4. Multiple Ordinal Regression and Odds Ratio for Membership in Class

Variables	Class 1 (moderate risk)	Class 2 (high risk)
	AOR* (CI95%)	AOR (CI95%)
Age of onset (>25)	1.2 (1.32–2.15)	1.4 (1.42–2.33)
Education level (under diploma)	2.2 (2.22–5.32)	1.38 (2.72–10.62)
Single	2.0 (1.7, 2.5)	1.7 (1.7, 4.8)
Sex (Female)	1.4 (1.74–6.52)	2.22 (1.74–7.64)
Unemployed	1.1 (1.4, 6.7)	2.5 (1.44–4.1)

* Adjusted Odds Ratio

Discussion

Result of LCA showed that, overall, 52%, 22% and 26% of participants with schizophrenia were divided into class 1, class 2 and class 3, respectively. Our findings showed that most patients with age of disorder onset under 25, were associated with high risk subgroup membership. This present finding seem to be consistent with other research which found that Schizophrenia mostly occurs in 15- to 25- year old males and 25- to 35-year old females (Gathaiya, 2011; Hussein, Jacob, & Sharour, 2016). A possible explanation for this finding might be that in case the onset of the disorder occurs in earlier ages, the period of recurrence and hospitalization will last more and may cause to squandered years and aggravate cognitive functions (Townsend, 2014). Schizophrenia may onset in early ages of life with chronic periods of relapse and also a decreasing level of functioning that leads to early school drop-out (Kazadi, Moosa, & Jeenah, 2008). We also observed that participants with schizophrenia who were unemployed were more likely to categorize in the highest-risk class

than members of the lowest-risk class. This is similar to findings of studies which proved that employment is an important factor to recovery of patients with schizophrenia in particular, and any other severe mental illnesses (Dunn, Wewiorski, & Rogers, 2008). Becoming independent by earning money from a job may increase self-esteem of patients and make them feel useful in family and society (Gunnmo & Fatouros Bergman, 2011). Owning a meaningful job is one of the most important requirements of patient's personal goals and aspirations as part of their well-being feeling. It is associated with their self-esteem and function and declining the negative, positive and depressive symptoms (Gunnmo & Fatouros Bergman, 2011). It has also financial advantages that helps with coping strategies with psychiatric symptoms, and at last it simplifies the mental illness recovery process (Sariah, 2012). Same as the other studies evidences, the more disorder grows, the poorer social and operational skills become, that may lead to unemployment, as in our study, higher rate of unemployment was seen in the relapse group (Chaurotia et al.). Additionally, Our findings indicated that female patients were more likely to belong to members of the highest-risk class than members of the lowest-risk class. This result differed from some published studies (Abdel-Baki et al., 2011; Chaurotia et al.). This may be due to the cultural background of them where it is difficult to live as a patient and there is a reduced tendency of marriage with this population. On the other hand, having a mental illness lable the stigma for the family of the patient and is considered taboo among people, therefore no one is willing to marry a person with a mental illness. The current study found that participants who belonged to members of class 2 were more likely to be single compared to members of either class 1 or class 3. This finding of the current study are consistent with those of Ali Hussein (2016) (Hussein et al., 2016) who found that half the samples were single (50%). This is consistent with findings from other studies showing that larger part of patients 73.3% were single and 12.2% were separated (San, Bernardo, Gómez, & Peña, 2013). Finally, our result indicated that patients who reported under high school diploma education level were more likely to belong to members of the lowest-risk class compared to members of the highest-risk class. In this study patients that experienced relapse were more likely to have lower levels of education (Kazadi et al., 2008). There are some limitations of this research that should be considered in future studies, was not being able to directly investigate the causal association between variables of interest and membership in multiple relapse risk groups; since the study was based on a cross sectional design. Besides, the data applied to the study were based on self-reports of participants and may therefore tend to recall and social desirability bias (Sharifi et al., 2017). One of the strength points of this study is that this research is implemented in the Razi Hospital that is the largest psychiatry hospital in Iran and the second point is that besides considering self-reports, in the case that medical records were incomplete or were not clear, we completed the information by questioning from families.

Conclusion

The high prevalence of relapse risk in the “high-risk” class raises an alarm for the policy makers in Iran to design and implement effective and timely interventions to prevent Schizophrenia relapse among this population and to their partners. These findings emphasize the importance of having targeted prevention programs for all domains of Age of onset, female and unemployed related. So, current study suggested that interventions should focus on these risk factors. Furthermore, Increasing the Job opportunities for participants with schizophrenia is warranted so as to prevent of schizophrenia disorder.

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