Factors associated with relapse among mentally ill patients attending military mental health clinics

Arafat khalaf Yousef Zubi. MD, Laith Taye Hasan Al-jarrah. MD, Malik Mansour Mohammed Al-Alwan .MD , Wafaa Tahseen Swalmeh. MD, Abeer Fayez Salem Habarneh. MD

Department of mental health - Royal Medical Services

Abstract

Objectives: To assess the prevalence and factors contributing to relapse among mentally ill patients attending military mental health clinics. Method: A cross sectional study was conducted on patients attending military mental health clinics at King Hussein Medical City, Princes Aisha Center, Prince Hashim Hospital and Prince Rashid Hospital. Socio-demographic data questionnaire, internalized stigma of mental illness scale (ISMI), medication adherence scale (MMAS-8), the list of threatening events questionnaire (LTE-Q), oslo's three items social support scale (OSSS-3) and the alcohol, smoking, and substance involvement screening test (ASSIST-3.0) were utilized for data collection. Data were analyzed using statistical package for social sciences (SPSS) version 22. Results: A total of 311 patients with mental illnesses were included in the study. Prevalence of relapse was 37.3%. Relapse was significantly associated with unemployment (OR = 1.84, 95% CI: 0.92 - 2.63), duration of diagnosis more than 5 years (OR = 2.42, 95% CI: 1.39 – 3.73), severe internalized stigma (OR = 3.12, 95% CI: 1.75 – 4.87) and low adherence to medication (OR = 2.14, 95% CI: 1.54 – 3.89). Conclusion: Around one third of the study participants had relapsed. Unemployment, duration of diagnosis more than 5 years, severe internalized stigma and low adherence to medication were significant predictors for relapse. Researchers suggest the need for future interventional studies focused on modifiable predictors of relapse such as stigma, employment, and medication adherence.

Keywords: Mental illness, relapse, predictors, stigma, medication adherence, substance abuse, stressful life events, social support.

Introduction:

Globally, mental illness is prevalent, affecting approximately 792 million people (10.7%) around the world (1). Anxiety disorders are the most common mental illness (3.76%) followed by depression (3.44%) (1). Mental illness causes substantial burden of disease (2). Recently, empirical evidence revealed that 7% of global disease burden and 19% of all years lived with disability compelled by mental illnesses (3). In Jordan, there is no recent and reliable data about the prevalence of mental illness. Based on world health organization report in 2011, it has been estimated that only 305 individuals per 100.000 citizens are diagnosed with mental illness (4).

Moreover, relapse is another important issue that increased burden of mental illness and place additional strain on health care systems (5, 6). Relapse is recognized as a barrier for recovery and rehabilitation for those suffered from mental illness. The term "revolving door syndrome" has emerged in literatures in the past decades described "the chronically mentally ill patients frequently readmitted to mental health settings because of inability to sustain life independently in the community" (7, 8). Relapse is common in mental disorders with high and varied rate of relapse 39.3-55.2% in bipolar disorders (9), 52-92% in schizophrenia (10), and 40-60% in substance abuse (11) , despite great improvement in services and quality and effectiveness of mental health treatment. This issue was also noticeable in developed countries with long standing community based mental health system; there was considerable proportion of patients recurrently admitted in psychiatric facilities (5). Therefore, relapse has been studied extensively in literatures, and attempts have been made to recognize its associated factors (10, 12-15).

In schizophrenic patients, medication non-adherence, substance abuse or addiction and economic issues (unemployment and cost of treatment) are considered to be key contributors to relapse (16-18). Unfortunately, relapse was documented among subgroup of patients with schizophrenia despite uninterrupted long-acting therapy (19). Therefore, Larry et al were studied the risk of relapse in schizophrenic patients on long-acting antipsychotic therapy to exclude medication adherence issue and found that risk of relapse was increased 4 fold in patients with 10 years or more of disease duration than those with 5 years or less disease duration (20). In bipolar patients, mixed type of bipolar disorder (21, 22) and medication non-adherence (23) were the leading causes of relapse. Furthermore, medication side effect, living alone, poor socioeconomic status, poor social support, stressful life events and delay in seeking care are speculated as common reasons for increased cases of relapse (24, 25).

In the course of mental illness, patients are experienced stigma which is serious risk factors associated with long term poor prognosis and increased morbidity and mortality (26). Stigma also impedes seeking help, initiation and treatment adherence (27). As regard large body of research that evaluated the factors associated with the relapse, relapse is a multidimensional and complex topic. However, there is still lack of consensus regarding prevalence and factors associated with relapse of mentally ill patients' in Jordan.

The current study aimed to assess the prevalence of relapse and to understand characteristics' of mentally ill patients with recurrent relapse which could update the development of appropriate services. Moreover, factors associated with relapse will be addressed in the present study including socio-demographic factors, stigma, social support, stressful life events, substance abuse and medication adherence which could help in improvement of relapse prevention modalities for these patients in Jordan.

Methods:

Study design and settings

A multicenter cross-sectional study design was employed. Study was conducted from Nov 2021 to Jan 2022 at four psychiatric outpatients clinics located at King Hussein Medical City, Princes Aisha Center, Prince Hashim Hospital and Prince Rashid Hospital. All four mentioned hospitals are military hospitals covered the Middle and North regions of Jordan.

Study population and sample size

All patients have a diagnosis of mental illness according to Diagnostic and Statistical Manual (DSM-5), confirmed by medical file and on follow up at any of the fourth previous mentioned outpatients' clinics were the source population. We included participants diagnosed with mental illness aged of 18 years and above, full of insight, patients and their caretaker willing to participate in the study, without cognitive impairment and have at least one year history of mental illness confirmed by patient file.

Sample size was determined based on computer program "Creative Research Systems Survey Software Calculator" by taking prevalence (P) from the previous WHO report (4). The estimated sample size required for the study was 302 patients. The accepted level statistical significance was P < 0.05.

Data collection instruments

The following valid instruments were used for data collection:

Socio-demographic data questionnaire: including age, sex, marital status, employment status, educational level, psychiatric diagnosis, and duration of the disease.

Internalized Stigma of Mental Illness Scale (ISMI): originally developed by Ritsher et al (2003), was used to measure the level of internalized stigma among patients. "It consisted of 29 statements, allowing calculation of the results in five domains: 1) alienation, 2) stereotype endorsement, 3) experience of discrimination, 4) social withdrawal, and 5) stigma resistance. The score in each domain will calculate by adding the item scores together and then dividing them by the total number of answered items. The resulting score ranged from 1 to 4. In the study, a four-category method was used to interpret each domain. The interpretations of the results were as follows: 1.00–2.00, minimal/no internalized stigma; 2.01–2.50, mild internalized stigma; 2.51–3.00, moderate internalized stigma; 3.01–4.00, severe internalized stigma" (28).

Medication Adherence Scale (MMAS-8) developed by Morisky et al., 2008: "it consists of 8 items. Response choices are ''yes'' or ''no'' for items 1 through 7 and Item 8 has a five point Likert response scale. Each ''no'' response is rated as 1 and each ''yes'' response is rated as 0 except for item 5, in which each ''yes'' response is rated as 1 and each ''no'' response is rated as 0. For Item 8, the code (0-4) has to be standardized by dividing the result by 4 to calculate a summated score. Total scores on the MMAS-8 range

from 0 to 8, with scores of 8 reflecting high adherence, 7 or 6 reflecting medium adherence, and <6 reflecting low adherence" (29).

The List of Threatening Events Questionnaire (LTE-Q) was developed by Brugha et al. in 1985. This comparatively short instrument composed of 12 items with dichotomous responses (i.e. yes/no) focusing on negative adverse events that happened over the past 12 months (30).

Oslo's three items social support scale (OSSS-3) developed by Dalgard 1996 was used to assess social support, "it has a range value of 3–14, which further categorized as ''poor social support'' 3–8, ''moderate social support'' 9–11, and ''strong social support'' 12 and above" (31).

The Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST-3.0) was adopted to assess the current use status of the participants. It developed by WHO to detect psychoactive substance use and related problems in primary care patients. Total score was classified as low, moderate and high risk level (32).

Data collection procedure

Data were collected by using face to face interview technique after assessing patients' insight by psychiatrist then; the researcher were read the questions to each participant to answer all questionnaires.

Ethical considerations

The study objectives were explained to the participants by the researchers and written informed consent was taken from both patients and their caretakers. Hence, the study nature may include some negative psychological consequences such as fear and anger, researchers made a focus on the following points: 1. all patients were informed about the right to quit the study during interview time 2. all patients were informed about the possible negative psychological consequences of the study 3. All data will gather under conditions of strict confidentiality and data were analyzed anonymously by patient ID number. Researchers were obliged to provide psychological support for any patients complaining from any psychological consequences. Ethical approval was obtained to conduct the study from Ethics Review Board at Royal Medical Services.

Relapse definition

Relapse was defined according to DSM-5 as "the patient should have a history of symptoms exacerbation or more than one admission history which was measured by reviewing the patient medical file and interviewing patients" (33). Patients were classified into two groups (relapse and non-relapse group) according the presence of relapse.

Statistical analysis

The collected data were edited, checked for missing data, coded and entered to SPSS version (22) statistical software for analysis. Descriptive statistics' used to present the results. Independent sample t test and Kruskal-Wallis test were utilized to compare groups with regard to socio-demographic characteristics and clinical related factors. Odd ratio was analyzed using bivariable and multivariable binary logistic regression analysis, the level of significance of association was determined at p value less than 0.05, and the strength of the association was presented by odds ratio with 95% confidence interval.

Results

Socio-Demographic characteristics of participants:

A total of 311 patients with mental illnesses were participated in the study, yielding a response rate of 88.85%. Mean of age of the participants was 42.81 with SD ± 13.47 and mean duration of the diseases was 7.58 with SD ± 5.14. The majority of the participants' were males 176 (56.6%) and almost half of the participants were single 152 (48.9%). Among all, 216 (69.5%) participants were non-employed regarding employment status and 149 (47.9%) participants had secondary level of education. Regarding diagnosis, most of the participants' 110 (35.4%) had bipolar affective disorder followed by 58 (18.6%) major depressive disorder, 54 (17.4%) schizophrenia, 41 (13.2%) psychosis, 40 (12.9%) anxiety disorders and the rest had other mental disorders such as eating disorders and personality disorders.

Participants were classified into two groups according to relapse. 195 (62.7%) participants were classified as non-relapse group and 116 (37.3%) as relapse group. Significant differences were found between groups with regard age, duration of the disease, educational level, employment status and type of diagnosis (P < 0.05). Mean of age in relapse group 46.65 (SD ± 12.29) was higher than non-relapse group 40.56 (SD ± 13.66). Moreover, mean of duration of the disease was higher in relapse group 11.10 (SD ± 5.79) than non-relapse group 5.52 (SD ± 3.30). 80.9 % of the participants in relapse group were non-employed compared to 62.8% of the participants in the non-relapse group. Diagnosis of schizophrenia/SAD was present with a

higher proportion in relapse group (34.4%), whereas major depressive disorder (23.5%), bipolar affective disorder (37.2%) and anxiety disorder (16.8%) were higher in non-relapse group. Table (1)

Prevalence of relapse:

The prevalence of relapse among mentally ill patients was 37.3%. Figure (1)

Clinical and psychosocial factors of participants:

Mean of Internalized Stigma of Mental Illness Scale (MMAS), Medication Adherence Scale, The List of Threatening Events Questionnaire (LTE-Q) and Oslo's three items social support scale (OSSS-3) were 2.33 (mild internalized stigma), 6.02 (moderate drug adherence), 1.57 (participants have experienced one to two stressful life events) and 9.37 (moderate social support) respectively.

Internalized stigma of mental illness across the groups showed significant difference (P=.001). Participants in relapse groups were experienced moderate internalized stigma (Mean=2.78), whereas participants in non-relapse group were experienced mild internalized stigma (Mean=2.07). With regard to medication adherence, participants in relapse group showed low drug adherence (Mean=5.29) whereas participants in non-relapse group showed moderate drug adherence (Mean=6.45). However, the two groups didn't show significant difference regarding number of threatening events and level of social support (P value were 0.233 and 0.466 respectively).

Regarding risk of substance abuse, participants showed moderate risk for tobacco (Mean= 14.54), low to moderate risk for cannabis (Mean = 3.91) and low risk for other substances. Both groups showed moderate risk for tobacco but, participant in relapse group showed higher mean score than non-relapse group despite the presence of both groups within range of moderate risk (P=0.001). Furthermore, significant difference was found between the groups with regard to the risk of abuse for hallucinogens but, mean score of both groups' lies in the same range of low risk for abuse. Table (2)

Factors associated with relapse:

Bivariable binary logistic regression variables showed that, being female, single, non-employed, had schizophrenia / schizoaffective disorder or psychosis or major depressive disorder or bipolar affective disorder, duration of diagnosis greater than 5 years, mild or moderate or severe internalized stigma, low or moderate adherence to medication and poor social support were variables found to have a p value less than 0.2. These variables fulfilled minimum requirements for further multivariable binary logistic regression.

Multivariable binary logistic regression variables showed that, being non-employed, duration of diagnosis more than 5 years, severe internalized stigma and low adherence to medication were variables found to be a statistically significant association with relapse at a p value < 0.05.

The odds of having relapse among participants who were non-employed were 1.84 times as compared to those who were employed (OR = 1.84, 95% CI: 0.92 - 2.63).

The odds of having relapse among participants who had duration of diagnosis more than 5 years were 2.42 times as compared to those who had duration of diagnosis less than or equal 5 years (OR = 2.42, 95% CI: 1.39 – 3.73).

The odds of having relapse among participants who had severe internalized stigma were 3.12 times as compared to those who had no internalized stigma (OR = 3.12, 95% CI: 1.75 – 4.87).

Lastly, the odds of having relapse among participants who had low adherence to medications were 2.14 times as compared to those who had high adherence to medication (OR = 2.14, 95% CI: 1.54 – 3.89). Table (3)

Table (1): Socio-demographic characteristics of the two groups of patients

Variables	Total (N=311)		Non-relapse group (N=195)		Relapse group (N=116)		P value
	Mean	SD	Mean	SD	Mean	SD	
Age	42.81	13.47	40.56	13.66	46.65	12.29	0.001*
Duration of disease	7.58	5.14	5.52	3.30	11.10	5.79	0.001*
	Frequency	%	Frequency	%	Frequency	%	P value
Gender							
Male	176	56.6	110	56.1	66	57.4	0.828**
Female	135	43.4	86	43.9	49	42.6	
Marital							

Single	152	48.9	95	48.5	57	49.6	0.852**
Married	159	51.1	101	51.5	58	50.4	
Employment							
Employed	95	30.5	73	37.2	22	19.1	0.001**
Non-employed	216	69.5	123	62.8	93	80.9	
Education							
Elementary	100	32.2	54	27.5	46	40.0	0.005**
Secondary	149	47.9	95	48.5	54	47.0	
High	62	19.9	47	24.0	16	13.0	
Diagnosis							
schizophrania/SAD	54	17.4	14	7.1	40	34.4	0.001**
psychosis	41	13.2	25	12.8	16	13.5	
MDD	58	18.6	46	23.5	12	10.4	
BAD	110	35.4	73	37.2	37	32.2	
anxiety disorders	40	12.9	33	16.8	7	6.1	
others	8	2.6	5	2.6	3	3.4	

*independent sample t test,   **Kruskal-Wallis test , SAD: Schizoaffective disorder, MDD: Major depressive disorder, BAD: Bipolar affective disorder, SD: standard diviation

Table (2): Distribution of clinical related factors of the two groups of patients

Variables	Total (N=311)		Non-relapse group (N=195)		Relapse group (N=116)		P value
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	
ISMI	2.33	0.91	2.07	0.83	2.78	0.88	0.001*
MMAS	6.02	1.29	6.45	1.20	5.29	1.08	0.001*
LTE-Q	1.57	1.47	1.50	1.61	1.70	1.18	0.233*
OSSS-3	9.37	2.75	9.33	2.57	9.42	3.04	0.446*
ASSIST-3.0							
Tobacco	14.54	9.44	12.95	9.21	17.26	9.25	0.001*
Alcohol	4.63	4.36	4.27	3.83	5.24	5.12	0.059*
Cannabis	3.91	3.18	3.91	2.64	3.92	3.96	0.982*
Cocaine	1.22	1.02	1.17	0.90	1.32	1.18	0.217*
Amphetamine	1.32	1.44	1.22	1.09	1.50	1.89	0.100*
Inhalant	1.10	0.92	1.08	0.98	1.13	0.83	0.632*
Sedatives	2.06	2.35	2.15	2.54	1.89	1.99	0.344*
Hallucinogens	1.09	1.48	0.96	1.23	1.31	1.82	0.049*
Opioids	0.48	0.99	0.44	0.93	0.54	1.08	0.374*
others	0.44	0.65	0.41	0.63	0.49	0.69	0.288*

ISMI: Internalized Stigma of Mental Illness Scale, MMAS: Medication Adherence Scale, LTE-Q: The List of Threatening Events Questionnaire, OSSS-3: Oslo's three items social support scale, ASSIST-3.0: The Alcohol, Smoking, and Substance Involvement Screening Test, *independent sample t test,   SD: standard diviation

Table 3: Bivariable and multivariable binary logistic regression analysis showing an association between relapse and associated factors among patients with mental illnesses

Explanatory variables	OR	95% CI	P value
Gender			
Male	1	1	
Female	1.67	0.92 - 2.86	
Marital status			
Single	2.14	1.28 - 3.45	
Married	1	1	
Employment			
Employed	0.78	0.45 – 1.64	

Non-employed	**1.84**	**0.92 - 2.63**	**0.015**
Diagnosis			
schizophrania/SAD	3.24	1.88 - 5.42	
psychosis	1.88	1.08 - 2.91	
MDD	2.32	1.22 - 3.66	
BAD	3.02	1.65 - 4.83	
anxiety disorders	1.68	0.87 - 2.35	
others	1	1	
Duration of diagnosis			
Less than or equal 5 years	1	1	
More than 5 years	**2.42**	**1.39 – 3.73**	**0.001**
ISMI			
No internalized stigma	1	1	
Mild internalized stigma	1.76	1.23 – 2.51	
Moderate internalized stigma	2.38	1.81 - 3.68	
Severe internalized stigma	**3.12**	**1.75 – 4.87**	**0.001**
MMAS			
low adherence	**2.14**	**1.54 – 3.89**	**<0.001**
Moderate adherence	1.28	1.02 – 1.68	
High adherence	1	1	
OSSS-3			
poor social support	1.83	1.09 – 2.33	
Moderate social support	0.96	0.45 – 1.21	
Strong social support	1	1	

ISMI: Internalized Stigma of Mental Illness Scale, MMAS: Medication Adherence Scale, OSSS-3: Oslo's three items social support scale, SAD: Schizoaffective disorder, MDD: Major depressive disorder, BAD: Bipolar affective disorder, CI: confidence interval, OR: odd ratio, chi-square = 12:872; df = 8; Hosmer and Lemeshow test = 0.116.

Figure 1: prevalence of relapse
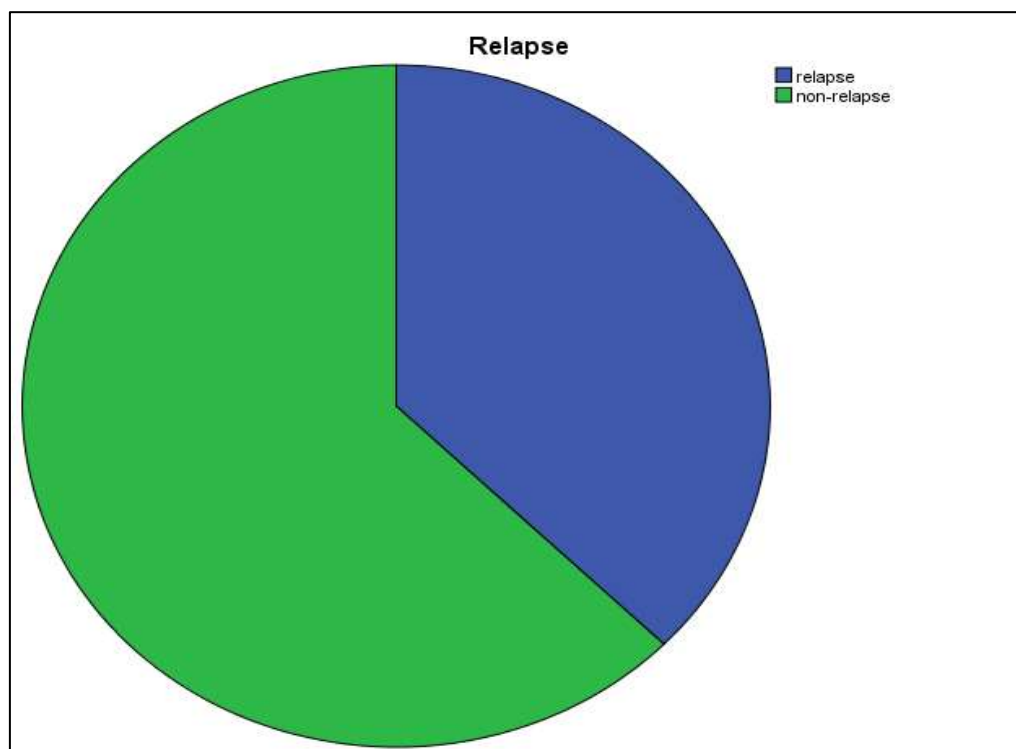
Discussion

Our study showed that the prevalence of relapse among mentally ill patients 37.3% which was lower than other studies conducted by Agenagnew and kassaw (70.2%), Moges et al (57.4%) and Lam et al (53%) (15, 17, 34) and this discrepancy could be explained by the differences in study settings, sample selection, tools and participants diagnosis. Moreover, the study included 54 schizophrenic patients with relapse prevalence 74% and 110 participants with bipolar affective disorder with relapse prevalence 33.7%. Similar results were reported in literatures for relapse prevalence of schizophrenic patients (10) whereas; the relapse prevalence of bipolar affective disorder participants was lower than reported in literature (9).

Many factors could contribute and increase the risk of relapse of mentally ill patients (12, 18, 24). In our study, we found that unemployment, duration of diagnosis more than 5 years, severe internalized stigma and low adherence to medication were significant predictors of relapse using logistic regression analysis. However, this study showed that socio-demographic variables such as age, gender, marital status, educational level, were not considered as predictors of relapse in this group of patients.

Interestingly, internalized stigma as a modifiable factor was the most significant predictor of relapse. This study reported that risk of relapse was increased more than three times among participants who had severe internalized stigma compared to those who had no internalized stigma. This is supported by Abdisa, E., Fekadu, G., Girma, S. et al study (35). Internalized stigma is a critical factor of relapse which delays seeking help, initiation and treatment adherence and increased morbidity (26, 27). Literatures reported significant positive correlation between internalized stigma and the duration of mental illness and this might due to the long-term poor social and occupational functioning (36, 37). Therefore, psychiatrists' have to assess stigma in clinical settings, using anti-stigma measures that is patient-centric, and promotes patients' social life. Moreover, social media should play a role in the de-stigmatization of psychiatric patients and mental illness as well.

This study found that the risk of relapse in patients who had duration of diagnosis more than 5 years was 2.42 times as compared to those who had duration of diagnosis less than or equal 5 years. This result is supported by Adebiyi, Mosaku, Irinoye, et al study (38). In addition, longer duration of mental illness increased feeling of uncontrollability, decrease hope of cure with medication and increased idealization of stigma (39).

This study found that low medication adherence as significant predictor of relapse and its increased risk of relapse by 2.14 times. This is supported by Agenagnew et al study (15). Adherence and compliance to medication is an important for the patient to control symptoms and prevent relapse. Medication side effects and distress associated with it and poor insight among mentally ill patients were recognized as factors associated with medication non adherence (40- 42). Logistic regression analysis in Fikreyesus et al study reported that the risk of developing psychotic relapse among participants who have experienced medication side effects was 1.83 times higher when compared to those who have never experienced medication side effects (24). Therefore, Increasing adherence to medication, psycho-education for patients and their families about the illness and medication side effects should be the center of attention to prevent relapse.

This study found that unemployment as another predictor for relapse. Moreover, majority of the patients in this study were unemployed (69.5%). Haslett et al reported that 75-90% of patients with schizophrenia are unemployed, and unemployment contributes to disease recurrence (43). Disability associated with mental illness affected patients' functionality and participation in society and increased risk of relapse by 3.72 times (15). Moreover, unemployment could affect patients' income. Therefore, rehabilitation and social skills' training is highly recommended to overcome patients' deficiencies in the daily life abilities.

Stressful life events in this study was not regarded as predictors of relapse in mentally ill patients whereas, this factor was recognized as a predictor of relapse in literatures (44, 45). This discrepancy might be due to differences of tools. Furthermore, mean score of stressful life events was 1.57 only which mean that majority of patients perceived one to two stressful life events as they reported.

Finally, substance abuse not regarded as predictors of relapse in mentally ill patients. Contrary, retrospective study of 22 patients with schizophrenia reported significant association between substance abuse and readmission rate to the hospitals (46).

Strength and limitations of the study

To our knowledge, this is first of kind study conducted at multicenter in Jordan that covered four large hospitals in the middle and north of Jordan. Moreover, this study used standardized and reliable questionnaires for data collection. Nevertheless, the current study also had some limitations: first, due to the cross-sectional nature of the study therefore, no conclusions can be drawn regarding causality and alternative

explanations of the results; second, the data were collected through an interviewer administered questioner so, the response could be prone to bias such as social desirability bias and recall bias. Third, variables such as comorbidities, patients or family income and presence of medical insurance were no included in the study.

Conclusion:

Around one third of the study participants had relapse with prevalence 37.3%. Unemployment, duration of diagnosis more than 5 years, severe internalized stigma and low adherence to medication were significant predictors of relapse as reported by logistic regression analysis. Researchers suggest the need for future interventional studies focused on modifiable predictors of relapse such as stigma, employment, and medication adherence.

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