Source details

International Journal of Social Psychiatry

Scopus coverage years: from 1955 to Present

Publisher: SAGE

ISSN: 0020-7640   E-ISSN: 1741-2854

Subject area: (Medicine: Psychiatry and Mental Health)

Source type: Journal

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Original Article

The biopsychosocial-spiritual factors influencing relapse of patients with schizophrenia

Margarita M Maramis[1], Muhammad Sofyan Almahdy[1],
Atika Atika[2], Cokorda Bagus Jaya Lesmana[3]
and Jakobus Gerick Pantouw[4] iD

Abstract

Objective: High relapse rate of patients with schizophrenia has a large impact on patients and their families that can be reviewed from biopsychosocial and spiritual factors. Determining all the potential risk factors of relapse in schizophrenia can help increase awareness of physicians, patients, and families. Physicians are the ones who examine patients and have responsibility to manage and educate them and expect to prevent relaps. This study analyze various biopsychosocial and spiritual factors affecting relapse occurrence in patients with schizophrenia.

Methods: Cross sectional observational analytic study on 226 subjects with schizophrenia in three places in East Java, Indonesia, namely Soetomo Academic Hospital Surabaya (33.2%), Menur Hospital Surabaya (32.7%), and Radjiman Wediodiningrat Mental Hospital Lawang (34.1%) that met the inclusion and exclusion criteria. Data collection including 33 biopsychosocial and spiritual factors and were analyzed using bivariate and multivariate logistic regression.

Results: Relapse rate within 1 year was 59.73%. There were 12 factors significantly affected the relapse of schizophrenia, namely history of physical disease of mothers during pregnancy ($p < .001$; $B = 27.31$; 95% CI 3.96–188.52), presence of trigger ($p < .000$; $B = 6.25$; 95% CI 2.61–14.96), negative beliefs ($p < .000$; $B = 4.94$; 95% CI 2.10–11.61), hereditary factors ($p < .001$; $B = 4.84$; 95% CI 1.93–12.10), insight ($p < .003$; $B = 4.27$; 95% CI 1.62–11.27), 1-year GAF Scale ($p < .015$; $B = 3.79$; 95% CI 1.30–11.09), response to treatment ($p < .006$; $B = 3.68$; 95% CI 1.45–9.36), family knowledge ($p < .011$; $B = 3.23$; 95% CI 1.31–7.93), history of head trauma ($p < .029$; $B = 3.13$; 95% CI 1.13–8.69), medication side effects ($p < .028$; $B = 2.92$; 95% CI 1.12–7.61), substance use history ($p < .031$; $B = 2.86$; 95% CI 1.10–7.45), and occupation ($p < .040$; $B = 2.40$; 95% CI 1.04–5.52).

Conclusions: The 12 factors of biopsychosocial-spiritual are determinant to predict the risk of relapse in patients with schizophrenia. These factors should be emphasized in psychoeducation for patients and their families to enable intervention and relapse prevention.

Keywords

Schizophrenia, biopsychosocial-spiritual factors, relapse

Introduction

Schizophrenia is a severe psychiatric disorder that has profound effects on about 1% of the world's population at some time in their lives. Many individuals with schizophrenia experience multiple relapses, which are associated with serious and potentially fatal outcomes (Lauriello, 2020). In Indonesia it is estimated that 6.7 per 1,000 household suffer of schizophrenia and 14.0% of Indonesian households have ever practised *pasung* (restraining and confinement of individuals with mental health problems) (Balitbangkes, 2018).

Relapse is a state of reappearance of schizophrenia symptoms in patients who have experienced remission within the last 1 year (Emsley et al., 2013). The term relapse is usually intended to be a symptom of worsening or relapse of positive symptoms rather than negative symptoms, and relapse interferes with the course of the disease (de Sena et al., 2003). Relapse in patients with

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schizophrenia makes the patient often consider himself to be a burden and less useful for the community. The economic burden and suffering that must be borne by patients with chronic schizophrenia is enormous. Nevertheless, patients who frequently experience relapse usually have a history of a longer duration of untreated psychosis than patients without relapse (Uçok et al., 2006).

Extended periods of relapse may cause progressive brain tissue loss after onset (Andreasen et al., 2013) which will aggravate the disease and make healing difficult, ultimately increasing personal and vocational skills deficits. Families also experience stress, anxiety, mutual blame, difficulty in understanding to accept the pain suffered by family members who have mental disorders (Simanjuntak & Daulay, 2006) the onset of depression and burnout in the family (Demirbas, 2017) and also negative stigma in the community against patients with schizophrenia and their families (Lippi, 2016). Relapse consider as one of the most costly aspects of schizophrenia.

There are several factors that also contributing to relapse in patients with schizophrenia, include personal risk, environmental risk, their caregivers, poor family support, stressful life events and substance use, adherence to antipsychotic medication, employment, and religion (Sariah et al., 2014). Therefore, research on the factors that cause relapse in patients with schizophrenia needs to be done comprehensively on biological, psychological, and spiritual factors to uncover which factors that strongly influence the relapse of patients with schizophrenia so that prevention steps can be taken.

Methods

This study was a quantitative observational analytic study with cross-sectional approach with data collection using a variety of questionnaires that have been validated into Indonesian language. Samples were taken by consecutive sampling technique, in which subjects who met the inclusion and exclusion criteria were selected until the required number of subjects was met according to the following formula $n = (5 \times V)$/prevalence. V is the number of independent variables to be studied (Dahlan, 2016).

Inclusion criteria: for patients: 18 to 60 years old, diagnosed with schizophrenia (ICD-10: F20) by psychiatrists, cooperative, relevant, and in remission at the Psychiatric Outpatient Unit. For patients' families: families of patient with schizophrenia who live together for at least 1 year and are caregivers of these patients who know the patient's history and accompanying the patient to visit the clinic, aged over 18 years without dementia, both are able to read and write, and willing to fill out informed consent and questionnaires. *Exclusion criteria*: incomplete data, and at any time refusing to be the subject of this study. Ethical clearance was released by Dr. Soetomo Academic Hospital number 0161/KEPK/IV/2018. Data were collected from three hospitals in East Java, Indonesia, the Dr. Soetomo Hospital, Surabaya, 75 (33.2%) subjects, Menur Mental Hospital, Surabaya, 74 (32.7%) subjects, and Dr. Radjiman Wediodiningrat Mental Hospital, Lawang, 77 (34.1%) subjects with a total of 226 subjects.

The variables studied were 33 factors that influenced the recurrence of schizophrenia patients, namely:

1. Biological factors (14 items) including age at first schizophrenia, gender, hereditary, history of head trauma, history of seizures or epilepsy, history of physical disorders of the patients' mother during fetal life of the patient, physical illness suffered during examination, patients drinking coffee or smoking or taking drugs, history of physical, and hormonal diseases of the mother after giving birth to the patient, types of schizophrenic disorders, route of antipsychotics administration, types of antipsychotics used, response to treatment, and side effects of the therapy.
2. Psychosocial factors (16 items) including level of education, employment, income, marital status, triggering factors, history of child abuse, schizoid personality traits, family knowledge on the factors of the patient's illness, family emotional support, financial and material support, patient's home distance to the hospital where the patient is examined, health insurance, GAF (Global Assessment Functioning) Scale during the examination, the best GAF Scale in the last 1 year, therapeutic rapport, and the patient's insight.
3. Spiritual factors (three items) including stigma and self-stigma, negative beliefs about diseases, treatment, and related ones, and the level of spirituality.

Data processing was done with the SPSS 24.0 application and XL Stat add in Microsoft Excel for Windows. Statistical analysis used the Kolmogorov-Smirnov normality test for age variables, univariate test, and bivariate chi-square test as well as multivariate logistic regression with backward stepwise tests.

Results

The normality test showed abnormal distribution of the patients' age and caregivers' age. The median age of the patients was 35 years, age range 19 to 90 years (mean 36.62 ± 11.54 years) and the median age of the caregivers/family was 50 years, age range 19 to 90 years (mean 48.05 ± 13.90 years). The relapse rate in the past year was 59.73%. The characteristics of the study subjects that consisted of 226 patients who met the inclusion criteria are shown in Table 1.

Bivariate analysis with chi-square test on 33 independent variables in Table 1 shows that there are 13 significant factors that affect relapse within 1 year, as in Table 2.

Table 1. Descriptive categorical data in the form of frequencies and percentages.

No.	Variables	Categories	Frequency (%)
1.	Age at having schizophrenia the first time (years)	⩽18	49 (21.68)
		>18	177 (78.32)
2.	Sex	Male	142 (62.83)
		Female	84 (37.17)
3.	Hereditary factor	Present	87 (38.50)
		Absent	139 (61.50)
4.	History of head trauma	Present	71 (31.42)
		Absent	155 (68.58)
5.	History epilepsy	Present	26 (11.50)
		Absent	200 (88.50)
6.	Thyroid or other chronic physical diseases	Present	23 (10.18)
		Absent	203 (89.82)
7.	Habit of substance use (caffeine, nicotine, narcotics, alcohol, other abusive drugs)	Present	163 (72.12)
		Absent	63 (27.88)
8.	History of physical disorders of the patients' mother during pregnancy	Present	12 (5.31)
		Absent	214 (94.69)
9.	History of hormonal dysfunction during pregnancy and post-delivery	Present	8 (3.54)
		Absent	218 (96.46)
10.	Type of schizophrenia	Specific[a]	124 (54.87)
		Non-specific[a]	102 (45.13)
11.	Route of antipsychotics administration	Oral	214 (94.69)
		Non-oral	12 (5.31)
12	Type of antipsychotic used	Typical	80 (35.40)
		Atypical	146 (64.60)
13.	Response to treatment	Poor	129 (57.08)
		Good	97 (42.92)
14.	Side effect of treatment	Present	68 (30.09)
		Absent	158 (69.91)
15.	Education	<High school	112 (49.56)
		High school-university	114 (50.44)
16.	Occupation	Absent	143 (63.27)
		Present	83 (36.73)
17.	Income	Absent/<RMW	211 (93.36)
		Present⩾RMW	15 (6.64)
18.	Marriage status	No/not yet	147 (65.04)
		Married	79 (34.96)
19.	Triggering factors	Absent	157 (69.47)
		Present	69 (30.53)
20.	History of child abuse	Present	50 (22.12)
		Absent	176 (77.88)
21.	Schizoid personality	Present	140 (61.95)
		Absent	86 (38.05)
22.	Family's knowledge on the disease and relapse	Less	81 (35.84)
		Adequate	145 (64.16)
23.	Emotional support from the family	Absent	30 (13.27)
		Present	196 (86.73)
24.	Financial and material support from the family	Absent	13 (5.75)
		Present	213 (94.25)
25.	Distance of patient's home to doctor's office (km)	>15	112 (49.56)
		⩽15	114 (50.44)
26.	Health insurance	Absent	41 (18.14)
		Present	185 (81.86)
27.	GAF Scale during examination	Poor	100 (44.25)
		Good	126 (55.75)

(Continued)

Table 1. (Continued)

No.	Variables	Categories	Frequency (%)
28.	GAF scale in a year	Poor	126 (55.75)
		Good	100 (44.25)
29.	Therapeutic rapport	Poor	90 (39.82)
		Good	136 (60.18)
30.	*Insight*	Poor	105 (46.46)
		Good	121 (53.54)
31.	Stigma and self-stigma	Present	153 (67.70)
		Absent	73 (32.30)
32.	Negative beliefs about disease, treatment, and related ones	Present	145 (64.16)
		Absent	81 (35.84)
33.	Level of spirituality	Poor	31 (13.72)
		Good	195 (86.28)

Note. RMW = regional minimum wage.
[a]Specific (paranoid, hebephrenic, catatonic, simplex); non-specific (other types, not-classified).

Table 2. Bivariate test results between 33 independent variables and relapse.

No.	Variables	Categories	Relapse in 1 year	No relapse in 1 year	Value		95% CI	
			n (%)	*n* (%)	*p*	PR	Min	Max
1.	Age at having schizophrenia the first time (years)	≤18	28 (57.14)	21 (42.86)	.799	0.95	0.72	1.24
		>18	107 (60.45)	70 (39.55)				
2.	Sex	Male	86 (60.56)	56 (39.44)	.780	1.04	0.83	1.30
		Female	49 (58.33)	35 (41.67)				
3.	Hereditary factor	Present	70 (80.46)	17 (19.54)	<.001	1.72	1.40	2.11
		Absent	65 (46.76)	74 (53.24)				
4.	History of head trauma	Present	56 (78.87)	15 (21.13)	<.001	1.55	1.27	1.88
		Absent	79 (50.97)	76 (49.03)				
5.	History epilepsy	Present	13 (50.00)	13 (50.00)	.295	0.82	0.55	1.22
		Absent	122 (61.00)	78 (39.00)				
6.	Thyroid or other chronic physical diseases	Present	14 (60.87)	9 (39.13)	1.00	1.02	0.72	1.44
		Absent	121 (59.61)	82 (40.39)				
7.	Habit of substance use (caffeine, alcohol, nicotine, drugs)	Present	110 (67.48)	53 (32.52)	<.001	1.70	1.23	2.35
		Absent	25 (39.68)	38 (60.32)				
8.	History of physical disorders of the patients' mother during pregnancy	Present	4 (33.33)	8 (66.67)	.071	0.54	0.24	1.22
		Absent	131 (61.21)	83 (38.79)				
9.	History of hormonal dysfunction during pregnancy and post-delivery	Present	4 (50.00)	4 (50.00)	.717	0.83	0.41	1.68
		Absent	131 (60.09)	87 (39.91)				
10.	Type of schizophrenia	Specific[a]	62 (50.00)	62 (50.00)	.001	0.70	0.56	0.87
		Non-specific[a]	73 (71.57)	29 (28.43)				
11.	Route of antipsychotics administration	Oral	130 (60.75)	84 (39.25)	.231	1.46	0.74	2.87
		Non-oral	5 (41.67)	7 (58.33)				
12.	Type of antipsychotic used	Typical	45 (56.25)	35 (43.75)	.479	0.91	0.72	1.15
		Atypical	90 (61.64)	56 (38.36)				
13.	Response to treatment	Poor	91 (70.54)	38 (29.46)	<.001	1.56	1.22	1.99
		Good	44 (45.36)	53 (54.64)				
14.	Side effect of treatment	Present	51 (75.00)	17 (25.00)	.003	1.41	1.15	1.72
		Absent	84 (53.16)	74 (46.84)				

(Continued)

Table 2. (Continued)

No.	Variables	Categories	Relapse in 1 year	No relapse	Value		95% CI	
			n (%)	n (%)	p	PR	Min	Max
15.	Education	<High school	68 (60.71)	44 (39.29)	.787	1.03	0.83	1.28
		High school university	67 (58.77)	47 (41.23)				
16.	Occupation	Absent	96 (67.13)	47 (32.87)	.003	1.43	1.11	1.85
		Present	39 (46.99)	44 (53.01)				
17.	Income	Absent/<RMW	126 (59.72)	85 (40.28)	1.00	1.00	0.65	1.53
		Present ≥ RMW	9 (60.00)	6 (40.00)				
18.	Marriage status	No/not yet	92 (62.59)	55 (37.41)	.29	1.15	0.91	1.46
		Married	43 (54.43)	36 (45.57)				
19.	Triggering factors	Absent	77 (49.04)	80 (50.96)	<.001	0.59	0.048	0.71
		Present	58 (84.06)	11 (15.94)				
20.	History of child abuse	Present	31 (62.00)	19 (38.00)	.84	1.05	0.82	1.35
		Absent	104 (59.09)	72 (40.91)				
21.	Schizoid personality	Present	86 (61.43)	54 (38.57)	.60	1.08	0.86	1.35
		Absent	49 (56.98)	37 (43.02)				
22.	Family's knowledge on the disease and relapse	Less	63 (77.78)	18 (22.22)	<.001	1.57	1.28	1.92
		Adequate	72 (49.66)	73 (50.34)				
23.	Emotional support from the family	Absent	19 (63.33)	11 (36.67)	.82	1.07	0.80	1.44
		Present	116 (59.18)	80 (40.82)				
24.	Physical and material support from the family	Absent	8 (61.54)	5 (38.46)	.88	1.03	0.66	1.61
		Present	127 (59.62)	86 (40.38)				
25.	Distance of patient's home to doctor's office (km)	>15	69 (61.61)	43 (38.39)	.66	1.06	0.86	1.32
		≤15	66 (57.89)	48 (42.11)				
26.	Health insurance	Absent	22 (53.70)	19 (46.30)	.39	0.88	0.65	1.19
		Present	113 (61.10)	72 (38.90)				
27.	GAF scale during examination	Poor	62 (62.00)	38 (38.00)	.63	1.07	0.86	1.33
		Good	73 (57.94)	53 (42.06)				
28.	GAF scale in a year	Poor	38 (61.29)	24 (38.71)	.88	1.04	0.82	1.31
		Good	97 (59.15)	67 (40.85)				
29.	Therapeutic rapport	Poor	70 (77.78)	20 (22.22)	<.001	1.63	1.32	2.00
		Good	65 (47.79)	71 (52.21)				
30.	*Insight*	Poor	75 (71.43)	30 (28.57)	.001	1.44	1.16	1.79
		Good	60 (49.59)	61 (50.41)				
31.	Stigma and self-stigma	Present	104 (67.97)	49 (32.03)	<.001	1.60	1.20	2.14
		Absent	31 (42.47)	42 (57.53)				
32.	Negative beliefs about disease, treatment, and related ones	Present	100 (68.97)	45 (31.03)	<.001	1.60	1.22	2.10
		Absent	35 (43.21)	46 (56.79)				
33.	Level of spirituality	Poor	20 (64.52)	11 (35.48)	.69	1.09	0.82	1.46
		Good	115 (58.97)	80 (41.03)				
	Total		135 (59.73)	91 (40.27)				

Note. RMW = regional minimum wage.
[a]Specific (paranoid, hebephrenic, catatonic, simplex); non-specific (other types, not-classified).
p < .05 (italics).

Thirteen factors that significantly affected relapse were subjected to multivariate testing using multivariate logistic regression binomial analysis with the following steps: selecting variables that would enter multivariate analysis using $p < .25$. Besides the 13 variable that significant, there were two additional variables that $p < .25$, that is, history of physical disorders in the mother during pregnancy of the patient and the type of drug administration, so that 15 variables were selected and 10 other variables were added which were observationally and clinically considered important by two expert psychiatrist, that is, history of epilepsy, GAF Scale in the past 1 year, current chronic physical illness, history of child abuse, stigma, therapeutic rapport, level of spirituality, marital status, personality, and health insurance. Furthermore, after coding, multivariate logistic regression analysis with backward stepwise

Table 3. Predictive model on relapse of patients with schizophrenia.

		Variables in equation						95% CI for Exp (*B*)	
		B	*SE*	Wald	df	Sig.	Exp (*B*)	Lower	Upper
Step 9									
1	Hereditary factor (4)	1.576	0.468	11.338	1	0.001	4.835	1.932	12.099
2	History of head trauma (9)	1.141	0.521	4.796	1	0.029	3.130	1.127	8.693
3	Response to therapy (7)	1.303	0.476	7.487	1	0.006	3.680	1.447	9.359
4	GAF Scale in a year (6)	1.332	0.548	5.911	1	0.015	3.789	1.295	11.088
5	History of physical disorders of the patients' mother during pregnant (1)	3.307	0.986	11.259	1	0.001	27.312	3.957	188.516
6	History of substance use (11)	1.052	0.488	4.648	1	0.031	2.863	1.100	7.449
7	Occupation (12)	0.873	0.426	4.198	1	0.040	2.394	1.039	5.516
8	Triggering factors (2)	1.832	0.445	16.922	1	0.000	6.247	2.610	14.955
9	Family knowledge (8)	1.171	0.459	6.510	1	0.011	3.225	1.312	7.928
10	Side effect of treatment (10)	1.072	0.488	4.815	1	0.028	2.920	1.121	7.605
11	*Insight* (5)	1.451	0.495	8.592	1	0.003	4.269	1.618	11.266
12	*Negative belief about disease, treatment, and related ones* (3)	1.597	0.436	13.403	1	0.000	4.937	2.100	11.607
	Constant	−9.660	1.594	36.739	1				

Note. The numbers in parentheses are the order from the highest (1) to the least influence (12).

method was performed on 25 variables to obtain a predictive model and has a good calibration ($p > .05$) using Hosmer and Lemeshow test $p = .718$ (Table 3).

Discussion

In this study, relapse rate was 59.73%. There was no difference in the likelihood of relapse between patients who were treated immediately compared with those who were treated late. Relapse examination was performed on patients who went to the hospital. In other words, only families who brought patients to the hospital. It was possible that relapsing negative symptoms were not considered as worsening that required hospital treatment. One-time relapse will lead to the possibility of subsequent relapse and residual symptoms in patients with schizophrenia (Jørgensen, 1998). However, a study in Hong Kong found that about 90% of patients with schizophrenia had relapse (Amelia & Anwar, 2013). This statement is confirmed by recent study that 41% of patients with schizophrenia were re-admitted to the hospital within 1 year. Likewise, a study in Korea also showed that 33.3% to 35.6% of patients with schizophrenia had readmission within 2 years (Lee et al., 2018).

In this study, a history of severe physical disturbance in the patient's mother when the patient was in his fetal life has a potential of 27 times to experience relapse compared to patients with schizophrenia with the patient's mother not experiencing physical disorders during pregnancy. The development of a baby's brain plays an important role in the occurrence of mental disorders later in life, especially

schizophrenia as well as its relapse. This is important to evaluate in patients so that realistic psychoeducation for the patient's prognosis can be given and treatment can be emphasized to minimize the relapse. A research in Finland found that pregnant women in the second trimester with viral infections had babies during the type A2 influenza epidemic in 1957 with potential to suffer from schizophrenia in adulthood. Those fetuses were developing and had a high risk of being treated in psychiatric hospitals with a diagnosis of schizophrenia (Torchin & Ancel, 2016).

Triggering factors are strong predictors and has four times potential for relapse in this study. Triggering factors sometimes are not readily recognized until the patient starts remission and recalls his/her experience at the start of the illness until the time of remission. This disclosure will increase the patient's insight and self-awareness of what is happening and can then be used to anticipate relapse by recognizing early signs of relapse. This finding is similar to that of Rosen who found that triggering factors are factors that do influence the relapse (Leff et al., 1992; Rosen & Garety, 2005; Vaillant, 1964).

Negative beliefs about schizophrenia has nearly five times potential for relapse in this study. Taking history on matters that influence the patient's understanding of the disease and drug culturally, spiritually, and religiously is important in the protection of relapse. In Riau Province District, Indonesia, 81.7% had negative perceptions (Sari et al., 2016) and surveys of community perceptions of severe mental disorders (schizophrenia) in general population at Tembelang village, Jombang, East Java, Indonesia, in 2012 found that perceived causes of schizophrenia

disorders were lack of faith (28%), witchcraft (19%), karma (14%) (Biro Koordinasi Kedokteran Masyarakat [BKKM] et al., 2012). Another study in Nigeria found that the majority (72.0%) of caregivers, especially without formal education supported the view that the supernatural is the most important cause in the etiology of schizophrenia (Igberase & Okogbenin, 2017). Research in India found that about 66% to 70% of the patients had at least one non-biomedical explanation model of supernatural type, while studies from other parts of the world reported the presence of supernatural explanation models in about 10% of the patients (Grover et al., 2014; Kate et al., 2012). Patients sought treatment first from a religious healer before came to hospital for a psychiatric consultation (Grover et al., 2014; Kate et al., 2012; Saravanan et al., 2007). Furthermore, there is some evidence to suggest that religion and religious practices influence the level of psychopathology, treatment adherence, and outcomes in patients with schizophrenia, and also influence social integration, suicide risk, and drug use (Borras et al., 2007).

This study found that patients with schizophrenia who had hereditary factors had a recurrence potential of almost five times compared to those who did not have hereditary factors. Although genetic intervention cannot be carried out yet, history taking about heredity needs to be done to anticipate relapse, so that it can be focused on the need for continuous and long-term treatment as well as regular follow-ups. At present, genetic and environmental factors are thought to influence the development of schizophrenia. Schizophrenia heredity is reported to reach up to 80%. If one parent has schizophrenia, the chance of the disease being inherited is 13%. If both parents, the chance is more than 20% (Hosak, 2013; Torchin & Ancel, 2016).

In this study, patient with poor insight has the potential of 4.2 times to experience a relapse. Insight is the first aspect that should be facilitated by the therapist to become better. It functions like an entrance for the therapist to help the patient. Good insights accompanied by other factors, for example, dosage forms, therapeutic responses, drug side effects, and availability, will improve compliance and better understanding of the disease, thus preventing relapse. Research by Aku et al. (2015) found that the poor level of insight and treatment adherence was strongly associated with more severe symptoms and increased levels of hostility, thereby reducing adherence in patients with schizophrenia. Analyzed from various aspects, insight can help understand and improve compliance behavior in clinical practice that will reduce the risk of relapse (Bitter et al., 2015).

In this study, poor GAF Scale score provides almost four times the potential for relapse than a good GAF Scale. This is consistent with a study from Almod et al. (2004) that found patients with schizophrenia who have a relapse have a low (bad) GAF Scale score with an OR = 0.93 (0.87–0.98). Functionality in patients with schizophrenia

is very important as the main outcome of treatment. Relapse causes functionality to be bad. This represents all symptoms of schizophrenia. A research by Bowyer with Cox proportional-hazard multivariate method provided the same result that the predictor of relapse in patients with schizophrenia is the increased symptom severity, where one indicator is poor GAF Scale value (Boyer et al., 2013).

In this study, poor response to treatment gives almost four times the potential for relapse compared to patients with schizophrenia with good response to treatment. Initial response within 2 weeks after antipsychotic administration is a good predictor for continued response in the first episode (Stauffer et al., 2011) and multiple episodes of psychosis (Agid et al., 2003). These factors affect therapeutic response and ultimately lead to relapse. There is no symptom from the patient at the first time of illness that can be used to predict with certainty whether the healing process will quickly or slowly improve, therefore treatment and adherence to treatment, follow-up, assessment and adjustment of treatment from clinicians become primary. A study by Carbon and Correl (2014) found that modifiable risk factors include treatment response, non-compliance with treatment, and comorbidity (substance abuse and depression). A part of the course of schizophrenia worsens even with treatment. A 20-year longitudinal study found that only 22.1% of patients experienced remission. Some of the factors that cause poor outcomes are type of diagnosis (Robinson et al., 1999) poor premorbid, male sex, earlier onset, longer illness, and long periods of absence (Carbon & Correll, 2014).

Low family knowledge has an effect on relapse in schizophrenia patients as much as three times compared with schizophrenia patients whose families have a high level of knowledge were found in this study. With adequate knowledge, patients, and families will certainly get the right medical perspective, not influenced by the layman's opinion about the disease, so they can choose and carry out the right treatment correctly and will get benefits in the form of good therapeutic outcomes and the patients will return to premorbid condition. Auni's study at Sardjito Hospital Yogyakarta in 2014 found a statistically significant difference in relapse between families of patients with a high level of schizophrenia knowledge and those with low knowledge; 20% and 5.5%, with a contingency coefficient of 0.217 (p = 0.030, 95% CI 0.00–0.063) (Bennett, 2014).

A history of head trauma has three times higher risk for recurrence compared to patients with schizophrenia who have never had head trauma were found in this study. Head trauma, especially one that causes nerve defects, will certainly worsen the course of schizophrenia. Therefore, in the first time finding or any acute exacerbation of schizophrenic disorder, the presence of organic factors needs to be considered so that appropriate treatment can be carried out and relapse can be reduced. A study by Abdel Malik et al.

(2003) in Canada found that the suffering of minor head injuries in as many as 67 subjects during their childhood of less than 10 years of age with $p = .04$ (OR 2.35; 95% CI 1.03–5.36) may play a role in the expression of schizophrenia in families with strong genetic predisposition.

In this study, side effects of treatment in patients with schizophrenia will increase recurrence by almost three times compared to those who do not experience it. Side effects also cause the patient not to take medication and relapse eventually recur. Side effects may present as visible and invisible symptoms. Therefore, in addition to observing the emergence of side effects of treatment, clinicians need to also ask about side effects that are not visible, for example, the mind becomes slower or empty, effects of sexual dysfunction, anxiety, etc., or conduct examination or measurement objectively, for example, measuring weight, testing blood prolactin level, filling out drug side effects questionnaires, and others. This is consistent with a study by Andreasen et al. (2013) who found that long-term antipsychotic administration and relapse often had an impact or side effect in the form of a reduction in brain volume so that the risk for relapse increased.

Patients who drink coffee or smoke were almost three times have higher chance to relapse than those who did not drink coffee or smoke were found in this study. The use of substances is a comorbid factor that aggravates schizophrenic disorder. It can be as a cause or result of schizophrenic disorder. Every patient who is seeking treatment needs to undergo screening or history taking for substance use. This was consistent with a study conducted by Cerimele and Katon (2012) who found that patients who smoked were more often hospitalized than those who did not smoke, so they had relapse more frequently and had higher PANSS measurement scores. A study by Cather et al. (2013) showed that patients with schizophrenia who ceased from treatment and smoked had potential to quickly experience relapse. Another study by Cakraborty et al. (2016) in India revealed that even small doses of cannabis use can cause relapse in patients with schizophrenia.

Patients with schizophrenia who do not have jobs have a risk 2.3 times higher to experience relapse compared with schizophrenia patients who have jobs were found in our study. It shows that jobs increase their self-esteem and makes them independent so that this becomes a protective factor against relapse. The patients can also learn to control themselves and manage their lives, and feel more meaningful in their lives, even though their schizophrenia still requires long-term treatment even for a lifetime. When patients engaged in different activities to earn a living, they felt free to spend their income because they did not need to ask others for financial support. In addition, by working they help earn a small income and they can use the money to buy drugs at times when the drugs are not available in pharmacies (Sariah et al., 2014).

The 12 biopsychosocial-spiritual factors have proven to be significant as a determinant for assessing the risk of relapse in patients with schizophrenia. However, the results of this study were limited to patients who came for treatment at the hospital. Relapse data were based on subjective questions on the patients' family, and partly based on the patients' medical record. Despite the limitations, it is prudent that both psychiatrists, patients, and families pay greater attention to these factors in order to assess the possibility of and prevent schizophrenia relapse. Therefore, knowledge about these factors need to be emphasized in psychoeducation for patients and their families to increase their awareness of the possible effects of biopsychosocial-spiritual factors on the patient's condition. The contribution of family members in intervening with unfavorable biopsychosocial-spiritual condition of the patient is key in relapse prevention, as family members are the ones that are likely to interact the most with the patient, and thus capable of identifying these factors. It may also be useful to quantify the effects of each factor, and create a scoring system to assess a patient's relapse susceptibility based on their biopsychosocial-spiritual condition, which would make it easier to identify the need for intervention before relapse occurs.

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