Symptomatic remission in first-episode psychosis and its predictors: a single-center study in Egypt

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Aim
The aim of the current study was to investigate the rates and predictors of symptomatic remission in patients presenting with first-episode psychosis 1 year after treatment initiation.
Patients and methods
A total of 102 participants aged 19–42 years who were consecutively enrolled into this study from October 2014 to November 2016 and who fulfilled the study inclusion criteria and completed 1-year of follow-up. Baseline and follow-up variables were collected via direct interview of the patients and their caregivers. In order to assess symptomatic remission, the standardized remission criteria for schizophrenia by the Remission in Schizophrenia Working Group were used, based on positive and negative syndrome scale.
Results
By the end of 1-year follow-up, 36.3% (*n*=37) of participants met the criteria for symptomatic remission. Logistic regression analysis showed that good premorbid functioning was found to be the only independent predictor of symptomatic remission.
Conclusion
In a cohort of Egyptian young people presenting with first-episode psychosis, the rate of symptomatic remission was low (36.3%) in comparison with previous cohorts conducted in the developing countries.

Keywords:
first-episode psychosis, outcome, predictors, symptomatic remission

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Introduction

Psychotic disorders such as schizophrenia are common, with 23.6 million prevalent cases worldwide in 2013 (Global Burden of Disease Study Collaborators, 2013). One in two people living with schizophrenia does not receive care for the condition (World Health Organization, 2013). The recovery rates (one in seven) (Jaaskelainen *et al.*, 2013) and associated disability (11th cause of disability worldwide in 2013) (Global Burden of Disease Study Collaborators, 2013), following a first episode of psychosis have not improved over the past 70 years under routine clinical care (Jaaskelainen *et al.*, 2013).

Although existing psychopharmacological treatments alone can reduce some symptoms, they have little impact on the outcome of the illness (Millan *et al.*, 2016). The annual national costs for the schizophrenia population ranged from US$94 million to US$102 billion worldwide, up to 1.65% of the gross domestic product (Chong *et al.*, 2016).

Furthermore, risk of all-cause mortality for psychotic disorders is twice (risk ratio, 2.54) that of the general population (Walker *et al.*, 2015). There is thus an urgent clinical and societal need for improving outcomes of psychosis (Fusar-Poli *et al.*, 2017).

Many patients with symptomatic remission do not achieve functional recovery. Symptomatic remission and functional recovery seem to be variable domains, representing two steps toward recovery that can but do not necessarily overlap. Nowadays, there is more interest in functional outcome, and treatment success is better defined by it (Peuskens and Gorwood, 2012).

There has been an encouraging and accelerated growth in research in first-episode psychosis (FEP). The growth in FEP research results from a confluence of findings pointing to the early (even *in utero*) origins of schizophrenia. There is also a broadening appreciation that while it is not yet possible to 'spot' schizophrenia from a variety of nonspecific and subtle 'impairments'

in social, linguistic, and cognitive performance, it is nevertheless evident that people later diagnosed with schizophrenia have been 'ill' for (in many instances) several years before they actually present for care (Perkins *et al.*, 2005).

Moreover, there is intriguing and provocative information from several high-risk studies, which suggests that effective, early intervention might (at least) forestall the onset of FEP (McGorry *et al.*, 2007). Such a perspective is important because it offers a glimpse of the potential for primary prevention of schizophrenia.

Patients and methods

Design and participants

The present study is a prospective observational study, conducted from October 2014 to November 2016; the participants were recruited from outpatient clinics and the inpatient departments of Mansoura University Hospital with the following inclusion criteria: *Diagnostic and statistical manual of mental disorders*, 4th ed., text revised (DSM-IV-TR) diagnosis of schizophrenia, delusional disorder, schizoaffective disorder, age of at least 18 years, patients of both sexes, and firstly diagnosed patients at the time of conduction of the study, and with the following exclusion criteria:

(1) DSM-IV-TR diagnosis of organic mental disorders.
(2) DSM-IV-TR diagnosis of substance-induced psychosis.
(3) Intellectual disability or illiterate patients which may interfere with the psychiatric interview.

Sample size

A convenient sample of 120 patients who are expected to attend the Psychiatry Department, Mansoura University Hospital fulfilling the inclusion criteria during the study period (1 year).

Assessment and measurements

Patients were evaluated at baseline (first visit), monthly visits for 6 months (second to sixth visits), then the last one 12 m from the baseline interview (seventh visit).

Baseline evaluations

The following sociodemographic and clinical data were collected from all patients or their relatives through direct interview: age, marital status: married or unmarried; and education: below secondary education, above secondary education; employment status: employed, unemployed, age of onset in years, type of psychosis: paranoid or nonparanoid schizophrenia, delusional disorder, or schizoaffective disorder. Type of medications prescribed at the initial visit (typical or atypical antipsychotics, depot, SSRIs or TCAs, the mood stabilizer prescribed and ECT), hospitalizations, duration of illness, duration of untreated illness (the duration from the deviation from the usual premorbid functioning to the time of initiation of medications).

The premorbid functioning as reported by the caregiver by asking them about the scholastic performance, adaptation to school, peer relationships, social aspects of life through the previous four life periods (childhood up to 11 years, early adolescence from 12 to 15 years, late adolescence from 16 to 18 years and adulthood 19 years and over), religious attitude, suicidal and aggressive behaviors, and family history of psychiatric disorders.

Diagnosis of cases was made according to the Structured Clinical Interview of DSM-IV-TR by the main investigator and two senior staff members. Also, urine screen test was done to all patients to exclude substance use disorder. Positive and negative syndrome scale (PANSS) were applied to all patients.

Follow-up evaluations

Monthly follow-up visits were held to assess the outcome of treatments, clinical progress of the patients, and side effects of medications, if any.

The following scales were applied to all patients:

PANSS (Kay *et al.*, 1987): monthly for 6 months (second to sixth visits) and then after 6 months (seventh visit). The Morisky medication adherence scale (MMAS-8) (Morisky *et al.*, 2008): after 1 month (second visit), 6 months (sixth visit), and 12 months (seventh visit) from the baseline visit. Simpson–Angus scale (Simpson and Angus, 1970): after 1 month (second visit), 6 months (sixth visit), and 12 months (seventh visit) from the baseline session.

Criteria for symptomatic remission

In order to assess symptomatic remission, the standardized remission criteria for schizophrenia by the Remission in Schizophrenia Working Group (Andreasen *et al.*, 2005) were applied. These criteria involved a severity criterion and a time criterion.

As regard the severity criterion, a score of mild (3) or less was required for all eight core symptoms of PANSS, including P1 delusions, P2 conceptual disorganization, P3 hallucinatory behavior, N1 blunted affect, N4 social withdrawal, N6 lack of spontaneity, G5 mannerisms/posturing, and G9 unusual thought concept. As regards the time criterion, the symptom severity mentioned above must have been maintained for at least 6 months.

Ethical consideration

The study was conducted after obtaining approval of the faculty ethics committee and written informed consent from the legal guardians of all participants. Confidentiality of the collected data was strictly kept.

Statistical analysis

Data were analyzed using SSPS statistical package, version 20. Qualitative variables were presented as numbers and percent; χ^2 or Fisher's exact test was used for group comparison, as appropriate crude odds ratio (COR) was calculated. Quantitative variables were tested for normality distribution by Shapiro test. Normally distributed variables were presented as mean±SD. Unpaired *t* test was used for group comparison. Nonparametric variables were presented as 'minimum–maximum' and Mann–Whitney test was used for group comparison.

Significant predictors of outcome on bivariate analysis were entered into logistic regression model and their adjusted odds ratio and confidence interval (CI) were calculated. *P* value less than or equal to 0.05 was considered as statistically significant.

Results

Table 1 shows that symptomatic remission is significantly higher in patient's age more than 30 as compared with patient's age less than 30 (COR=3.8, 95% CI=1.63–8.9), married patients as compared with unmarried patients (COR=4.4, 95% CI=1.8–10.4), and in working patients as compared with nonworking patients (COR=63.7, 95% CI=13.6–298).

Table 2 shows that symptomatic remission is significantly higher in patients with age at onset of diagnosis more than 30 as compared with patients with age at onset of diagnosis less than 30 (COR=5.3, 95% CI=2.2–12.9) and patients with shorter duration of untreated illness as compared with patients with longer duration of untreated psychosis (COR=13.4, 95% CI=4.5–39.3). Patients with good premorbid functioning as compared with patients with bad premorbid functioning (COR=87.1, 95% CI=11.1–682) and patients with negative family history as compared with patients with positive family history (COR=8.5, 95% CI=2.7–26.7).

The logistic regression analysis demonstrates that the good premorbid functioning is the only independent predictor of symptomatic remission with adjusted odds ratio of 87.1 (Table 3).

Table 4 shows significant difference between remitted and nonremitted patients in MMAS score ($P \leq 0.001$).

Table 5 shows that rates of remission in schizophrenia is 32%, in delusional disorder is 38%, and in schizoaffective disorder is 40%.

Table 1 Symptomatic remission according to sociodemographic data

Items	Total	Remitted [*n* (%)]	χ^2 (*P* value)	COR (95% CI)
Overall	102	37 (36.3)		
Sex				
Male (r)	53	16 (30.2)		
Female	49	21 (42.9)	1.76 (0.18)	1.7 (0.76–3.9)
Age (years)				
<30 (r)	62	15 (24.2)		
≥30	40	22 (55.0)	9.98 (0.002)	3.8 (1.63–8.9)
Marital status				
Married	36	21 (58.3)		
Unmarried (r)	66	16 (24.2)	11.71 (0.001)	4.4 (1.8–10.4)
Educational level				
Primary and preparatory (r)	54	23 (42.6)		
Secondary and university	48	14 (29.2)	1.98 (0.16)	1.8 (0.8–4.1)
Occupational status				
Nonworker (r)	53	2 (3.8)		
Worker	49	35 (68.2)	52.38 (≤0.001)	63.7 (13.6–298)

CI, confidence interval; COR, crude odds ratio.

Table 2 Symptomatic remission according to clinical data

Items	Total (102)	Remitted (37) [*n* (%)]	χ^2 (*P* value)	COR (95% CI)
Diagnosis				
Firstly diagnosed (r)	75	22 (29.3)		
Not firstly diagnosed	27	15 (55.5)	5.06 (0.025)	3.01 (1.2–7.5)
Age at the onset of diagnosis (years)				
<30 (r)	66	15 (22.7)		
≥30	36	22 (61.1)	18.84 (≤0.001)	5.3 (2.2–12.9)
Duration of untreated illness (years)				
<1	53	32 (60.4)		
>1 (r)	49	5 (10.2)	27.72 (<0.001)	13.4 (4.5–39.3)
Current medication	27	7 (25.0)	–	1
First generation/second generation	51	23 (45.1)	3.1(0.07)	2.4(0.9–6.8)
Combined	24	7 (30.4)	0.2(0.66)	1.3 (0.4–4.5)
Hospitalization during study				
No (r)	34	14 (43.8)		
Yes	68	23 (32.9)	1.12 (0.29)	0.6 (0.26–1.5)
Premorbid functioning				
Bad (r)	47	1 (2.1)		
Good	55	36 (65.5)	43.9 (<0.001)	87.1 (11.1–682)
Family history				
Yes (r)	65	4 (10.8)		
No	37	33 (50.8)	16.2 (≤0.001)	8.5 (2.7–26.7)
Suicidal thoughts				
Yes (r)	72	9 (30.0)		
No	30	28 (38.9)	0.72 (0.39)	1.5 (0.6–3.7)
Aggressive behavior				
Yes (r)	48	21 (38.9)		
No	54	16 (33.3)	0.34 (0.56)	0.78 (0.34–1.76)
Religious attitude				
Yes	61	20 (48.8)		
No (r)	41	17 (27.9)	4.63 (0.031)	2.5 (1.07–5.6)
Type of psychosis				
Schizophrenia	51	16 (32.3)		
Delusional disorder	26	10 (38.4)		
Schizoaffective disorder (r)	25	11 (44)	0.47 (0.79)	0.65 (0.23–1.85)

CI, confidence interval; COR, crude odds ratio.

Table 3 Logistic regression analysis of independent predictors of remission

	Multivariate regression		
Independent predictors	β	*P* value	AOR (95% CI)
Premorbid functioning			
Bad (r)	4.468	<0.0001	87.1 (11.3–682)
Good			
Constant		–3.89	
Model χ^2		53.03, *P*≤0.001	
% Correctly predicted		80.4	

AOR, adjusted odds ratio; CI, confidence interval.

Table 6 shows that religious attitude is significantly correlated to MMAS score of high adherence.

Table 7 shows that good premorbid functioning is significantly correlated to lower PANSS negative subscale score and not significantly correlated to lower positive subscale score.

Discussion

The percentage of remitted patients in this study is 36.3%, which is lower than 47% remission rate of the Hong Kong study conducted by Tang (2012). This may be due to the higher numbers of patients with DSM-IV-TR diagnosis of nonparanoid schizophrenia (24 cases of 102 as compared with eight of 96 cases in the Hong Kong study) and delusional disorder (26 cases of 102 as compared with four of 96 cases in the other study), which are characterized by lower remission rates than the other psychotic disorders.

The remission rates was 39.2% in the study conducted by Gaebel *et al*. (2014) within the German Research Network on Schizophrenia after a follow up of 166 patients of schizophrenia for 1 year (111 completers). The remission rate was 36% in the OPUS trials after a

Table 4 Comparison between remitted and nonremitted as regards positive and negative syndrome scale scores, SFQ scores, SF36 scores, Simpson–Angus scale, Morisky medication adherence scale, and GAF scores on the first visit

Items 1st	Remitted (37)	Not remitted (65)	*t* test	*P* value
PANSS 1st visit				
PANSS positive subscale	20.62±2.28	19.80±2.25	1.76	0.082
PANSS negative subscale	15.24±4.91	16.89±5.83	1.53	0.13
PANSS general psychopathology	23.72±4.56	25.49±4.93	1.78	0.078
SAS and MMAS 1st visit				
SAS	1 (0.00–8.00)	1 (0.00–10.00)	0.66	0.510
MMAS total score				
Medium	7 (18.9%)	57 (87.7%)	47.7	≤0.001
High	30 (81.1%)	8 (12.3%)		

MMAS, Morisky medication adherence scale; PANSS, positive and negative syndrome scale; SAS, Simpson–Angus scale. Significant difference between remitted and nonremitted patients in MMAS score ($P \leq 0.001$).

Table 5 Rates of remission according to the type of psychosis

Type of psychosis	Total (102)	Remitted (37) [*n* (%)]	χ^2 (*P* value)
1,2 schizophrenia	61	20 (32)	
3 delusional disorder	13	5 (38)	5.37 (0.251)
4 schizoaffective disorder	10	4 (40)	

Table 6 Relation between religious attitude and Morisky medication adherence scale total score

	Religious attitude [*n* (%)]			
Items	Yes	No	χ^2	*P* value
MMAS total score				
Medium	15 (26.3)	42 (73.7)	10.35	0.001
High	26 (57.8)	19 (42.2)		

MMAS, Morisky medication adherence scale.

2-years follow up of 369 patients with first-episode schizophrenia (67% completers) (Petersen *et al.*, 2008).

As regards the current study, the following sociodemographic and clinical variables were found to be significantly associated with symptomatic remission: older age at onset of diagnosis, being married, good premorbid functioning, shorter duration of untreated illness, scores on MMAS that indicates high adherence to medications, negative family history of schizophrenia spectrum disorders, and good occupational status. As regards the older age at onset of diagnosis, its association with symptomatic remission coincides with the results of the study of Crumlish *et al.* (2009), who stated that later age at onset had been considered as a predictor of symptomatic remission in schizophrenia.

The association of marriage with symptomatic remission was confirmed in this study and the following studies: The Singapore cohort (Tsoi & Kua, 1992), the Nottingham cohort (Harrison *et al.*, 1996), and the South African cohort (Emsley *et al.*, 2006) which noted better outcome clinically and functionally among patients who are married. However, the marital status is not a parameter of outcome among all other first-episode studies (Bottlender *et al.*, 2003).

The findings of the significant association of shorter duration of untreated illness to symptomatic remission in this study is in line with the results of the study carried out by Craig *et al.* (2000), who found that the shorter interval before starting medications had been consistently linked to symptomatic remission, and stated that seven short-term studies, three medium-term studies, and two long-term studies confirmed this association.

In this study, there is a significant association between good premorbid functioning and occupational status at baseline and symptomatic remission, and this is consistent with the results of the study conducted by Malla *et al.* (2006), who proposed that bad premorbid functioning expected decreased probability of remission. Lambert *et al.* (2009) reported that occupational status at baseline and premorbid functioning were significantly associated with remission.

The findings of significant association between high adherence to medications and symptomatic remission were confirmed by this study and the study conducted by Petersen *et al.* (2008), who stated that treatment adherence was a predictor of a shorter time or more probability of remission. The significant association

Table 7 Relation between premorbid functioning and positive and negative subscale scores

	Premorbid functioning			
Items	Bad	Good	χ^2	*P* value
PANSS negative subscale	18.81±5.82	10.92±4.35	7.801	<0.001
PANSS positive subscale	16.78±4.22	15.94±3.98	1.035	0.303

PANSS, positive and negative syndrome scale.

between remission and negative family history in this study was confirmed by Rosen *et al*. (2011) in her retrospective study of predicting recovery from schizophrenia.

When all these potential predictors were entered into the baseline multivariate model, only the good premorbid functioning was the independent predictor of symptomatic remission in this study, and this coincides with results of the Hong Kong study carried out by Tang (2012), with the difference being that the duration of untreated psychosis also was a predictor of symptomatic remission besides the good premorbid functioning in the Hong Kong study. In the current study, duration of untreated illness was the variable and not duration of untreated psychosis, and it is recognized that it is more related to the functional outcome in most studies.

Conclusion

Using multivariate regression analysis model of the potential predictors of symptomatic remission, it revealed that good premorbid functioning was the only independent predictor of symptomatic remission in this study.

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Conflicts of interest

There are no conflicts of interest.

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