Depression in schizophrenia is associated with higher incidence of relapse and rehospitalization (Herz and Lamberti, 1995), lower level of social functioning and quality of life (Sim et al., 2004), and increased suicidality (Fenton, 2000).

To study depression and depressive symptoms in first episode psychosis (FEP) is relevant, since the highest prevalence rate of suicide and suicidal behavior is found during the first years after start of treatment (Melle et al., 2006; Verdoux et al., 2001) and the rate of suicidal behavior during the early phase has been shown to rise parallel with the severity of depressive symptoms (Gonzalez-Pinto et al., 2007). The time course of depression in this context, i.e., whether it starts before, after, or at the same time as the psychotic symptoms and the consequences of this has been under debate (Birchwood et al., 2000; Hafner et al., 1999). Furthermore, the resolution of psychotic symptoms has been shown to play a critical part in the future course of the illness (Melle et al., 2008).

**Abstract:** The aims of this study were to examine the prevalence and pattern of lifetime Diagnostic and Structural Manual of Mental Disorders (fourth version) major depressive episodes, and the relationship between patient characteristics and current severity of depressive symptoms in first episode psychosis patients (FEPP). A total of 122 FEPP from the ongoing longitudinal thematically organized psychosis research study were included at first treatment. A total of 58 patients (48%) had experienced one or more major depressive episodes; 21 (17%) before onset of psychosis and 37 (30%) during or after onset of psychosis. Poor premorbid childhood adjustment, substance abuse, and excitatory symptoms at start of treatment were statistically significantly associated with higher current severity of depressive symptoms. Alcohol use was significantly associated with current severity of depression in men, while excitatory symptoms were associated in women. Thus depressive symptoms are frequent among FEPP, with indications of gender specific differences in patient characteristics that might imply different approaches to treatment.

**Key Words:** First episode psychosis, depression, schizophrenia, gender differences.

Depression and Depressive Symptoms in First Episode Psychosis

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Few studies have examined depressive symptoms in FEP patients. The prevalence rate of depression in early psychosis varies widely across published studies (17%–83%) (Hafner et al., 2005; Koreen et al., 1993; Sim et al., 2004; Addington et al., 1998; Bottlender et al., 2000) and is probably due to heterogeneity in the study populations, variation of assessment tools and whether it is the depressive affect, the symptom or the syndrome that is assessed.

Previous studies in schizophrenia spectrum disorders have shown men to have earlier onset, poorer premorbid functioning and different premorbid behavioral predictors of psychosis such as more negative symptoms and cognitive deficits with greater structural brain and neurophysiological abnormalities (Leung and Chue, 2000). Further knowledge about the prevalence, time course, gender differences, and possible contributing factors regarding the development of depression in relation to psychotic symptoms are thus needed.

The main aims of the current FEP study were as follows:

1. Describe the time course of lifetime Structured Clinical Interview for DSM-IV (SCID-I) verified major depressive episode (MDE).
2. Examine differences in demographic and clinical characteristics between patients with and without a lifetime history of MDE.
3. Examine how different patient characteristics contribute to current depressive symptoms as measured by the Calgary Depression Scale for Schizophrenia (CDSS) with an emphasis on gender differences.

**METHODS**

**Subjects**

From July 2004 to July 2007, 122 FEP patients from the 3 main psychiatric treatment centers in Oslo were included consecutively in the ongoing longitudinal thematic organized psychosis research study (TOP). The criteria were (1) age 18 to 65 years and (2) a first episode of a nonaffective psychosis according to Diagnostic and Structural Manual of Mental Disorders, fourth version (DSM-IV). The diagnostic distribution was as follows: schizophrenia 62 (50.8%), schizoaffective disorder 11 (9%), schizoaffective disorder 6 (4.9%), brief psychosis 6 (4.9%), delusional disorder 5 (4.1%), psychosis not otherwise specified 32 (26.2%). Exclusion criteria were a history of organic brain disorder, a significant comorbid medical condition, or an IQ of less than 70.

Patients were eligible for inclusion up to 52 weeks following the start of first adequate medication or hospitalization for psychosis. They were not considered as FEP patients if they previously on any occasion had been treated with antipsychotic medication in adequate dosage for more than 12 weeks or until remission. Being psychotic was defined as having a rating of 4 or more on the positive and negative symptom scale (PANSS) items P1, P2, P3, P5, P6, or G9 for more than one week. The mean age of the patients was 28.3 (SD: 9.2). 44 (36%) were women, 96

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**ISSN:** 0022-3018/10/19801-0067

**DOI:** 10.1097/NMD.0b013e3181c81ec0
(78.7%) were single, 16 (13.1%) were married/cohabiting, 10 (8.2%) were divorced/separated. Mean years of education were 12.7 (SD: 2.8) and median duration of untreated psychosis (DUP) were 38 weeks (range: 0–1040). All patients gave written informed consent and the study was approved by the regional research ethics committee.

Assessment

Measures

Diagnosis was set according to the SCID-I interview for the DSM-IV (American Psychiatric Association, 1994). Current psychotic symptom level was measured with the SCI-PANSS (Kay et al., 1987) and the global assessment of functioning scale (GAF) (Jones et al., 1995) split version. Current severity of depressive symptoms was assessed using the CDSS (Addington et al., 1990). Number of lifetime MDE was defined according to SCID-I. Since the criteria for this diagnosis comprises items that could be difficult to distinguish from negative symptoms or cognitive dysfunction associated with schizophrenia, we chose to be as strict as possible and thus only consider MDE (not mild or moderate). We registered MDE up until one year before the recorded onset of the first psychotic episode as MDE with onset before psychosis, and MDE with onset within the same year or after the onset of the first episode as MDE with simultaneous onset or onset after psychosis. DUP was measured following the criteria described by Larsen et al. (1998). Premorbid adjustment was measured with the premorbid adjustment scale (Cannon-Spoor et al., 1982). The premorbid phase is defined as the time from birth until 6 months before onset of psychosis. It measures social and academic functioning in childhood, early adolescence, late adolescence, and adult life. The Alcohol Use Disorders Identification Test (AUDIT) (Saunders et al., 1993) was used to screen for problem drinking, and use of illegal drugs was assessed with Drug Disorders Identification Test (Berman et al., 2005).

Procedures

The patients were interviewed by trained psychologists and psychiatrists at the same time as the SCID-I was administered. The investigators had all completed the general training and reliability program in the thematic organized psychosis research study. For DSM-IV diagnostics, mean overall kappa with training videos was 0.77, and mean overall kappa for a randomly drawn subset of actual study patients was also 0.77 (95% confidence interval [CI]: 0.60–0.94). Interrater reliability, measured by the intraclass correlation coefficient (1.1), was for the PANSS positive subscale 0.82 (95% CI: 0.66–0.94), for the PANSS negative subscale 0.76 (95% CI: 0.58–0.93), the PANSS general subscale 0.73 (95% CI: 0.54–0.90), the GAF symptom scale 0.86 (95% CI: 0.77–0.92), and the GAF functioning scale 0.85 (95% CI: 0.76–0.92).

ANALYSIS

Statistical analysis was performed using SPSS for Windows (version 16.0). Preliminary analysis was performed to examine the distribution of each variable and to test all measures for normality. Only the DUP required transformation to its natural logarithm (Ln[DUP + 1]). The 5-factor model of the PANSS was used for the analysis (Bentsen et al., 1996). Descriptive statistics for the whole sample were obtained using proportions, means or medians according to the measurement type and distribution. Independent sample t tests were used to assess potential differences between groups on demographic and symptom variables. Pearson correlation coefficients were used to show how the variables were associated within the groups. Correlations were initially performed for the whole sample and subsequently divided by gender. Significance level was set to p < 0.05; all tests were 2-tailed. Hierarchical multiple linear regression analysis on the whole sample and divided by gender were performed to study what independent variables influenced the current severity of depressive symptoms measured by the CDSS.

### TABLE 1. Mean and SD of Patient Characteristics and Their Correlations With CDSS Total Score for the Whole Sample and Divided by Gender

|                         | CDSS                              |                          |                          |                          |
|-------------------------|-----------------------------------|--------------------------|--------------------------|--------------------------|
|                         | Mean (SD) Total                   | r                       | Female (n = 44)           | Male (n = 75)            |
| Age                     | 41.13 (11.99)                     | −0.05                    | −0.23                    | 0.05                     |
| GAF symptom             | 7.41 (7.32)                      | −0.24*                   | −0.22                    | −0.26*                   |
| GAF function            | 44.54 (13.48)                    | −0.03                    | 0.05                     | −0.20                    |
| PANSS                   |                                   |                          |                          |                          |
| Positive                | 12.92 (4.55)                     | 0.04                     | −0.08                    | 0.14                     |
| Negative                | 20.04 (7.70)                     | 0.16                     | 0.25                     | 0.25*                    |
| Excitative              | 7.76 (2.54)                      | 0.30**                   | 0.54**                   | 0.13                     |
| Depressive              | 11.63 (3.69)                     | 0.62**                   | 0.56**                   | 0.67**                   |
| Cognitive               | 5.10 (1.82)                      | 0.02                     | 0.10                     | 0.04                     |
| Audit score             | 7.41 (7.32)                      | 0.25**                   | 0.23                     | 0.31**                   |
| Dudit score             | 6.96 (10.11)                     | 0.19*                    | 0.36*                    | 0.17                     |
| PAS                     |                                   |                          |                          |                          |
| Childhood social        | 1.21 (1.44)                      | 0.33**                   | 0.30*                    | 0.27*                    |
| Childhood academic      | 1.70 (1.25)                      | 0.24**                   | 0.40**                   | 0.30**                   |
| Early adolescence social| 1.30 (1.36)                      | 0.32**                   | 0.18                     | 0.29*                    |
| Early adolescence academic | 2.09 (1.36)                 | 0.32**                   | 0.45**                   | 0.26*                    |
| DUP (median/range)      | 38 (0–1040)                      | 0.19*                    | 0.41**                   | 0.02                     |

*Correlation is significant at the 0.05 level (2-tailed).
**Correlation is significant at the 0.01 level (2-tailed).
independent variables entered were chosen on the basis of significant associations from preliminary bivariate analysis of their associations to CDSS scores.

RESULTS
A total of 58 patients (48%) met the criteria for a lifetime history of at least one MDE. Twenty-seven (22%) had experienced recurrent MDE. The analysis revealed no differences between the group with and without a lifetime MDE concerning demographic variables such as age, marital status, education or in clinical measures as GAF, premorbid adjustment scale, or PANSS with the expected exception of the depressive factor score.

Twenty-five patients (21%) met the criteria for a MDE at the time of inclusion, and there were no gender differences within this group. There were no differences in age, marital status, or years of education between the group who met the MDE criteria at time of inclusion and the group who did not.

Twenty-one patients (17%) had experienced a MDE more than a year before onset of FEP, while 37 patients (30%) experienced their first MDE during or after onset. A larger proportion of females 13 (30%) compared with males 8 (10%) \(p = 0.01\) had experienced a MDE before their first episode of psychosis. Thirteen females (30%) compared with 12 males (15%) \(p = 0.06\) had experienced more than one MDE.

The associations between central clinical variables and CDSS for the total sample and divided by gender are displayed in Table 1. To estimate the independent contribution to the CDSS total score for each of the variables we carried out a multiple hierarchical linear regression analysis (Table 2). The included variables explained a total of 28% of the variance in CDSS.

| TABLE 2. Blockwise Multiple Regression Analysis of the Relationship Between Patient Characteristics and CDSS Total Score \((n = 119)\) |
|---|---|---|---|---|---|
| Gender | 2.686 | 0.819 | 0.001 | 1.061 | 4.311 |
| Age | 0.028 | 0.045 | 0.535 | -0.062 | 0.118 |
| PAS childhood social | 0.158 | 0.230 | 0.493 | -0.299 | 0.616 |
| PAS childhood academic | 0.321 | 0.250 | 0.201 | -0.174 | 0.816 |
| PAS early adolescence social | 0.133 | 0.235 | 0.572 | -0.333 | 0.600 |
| PAS early adolescence academic | 0.285 | 0.449 | 0.527 | -0.606 | 1.715 |
| AUDIT | 0.156 | 0.058 | 0.008 | 0.042 | 0.271 |
| DUDIT | 0.003 | 0.045 | 0.952 | -0.087 | 0.092 |
| PANSS positive | -0.022 | 0.091 | 0.812 | -0.201 | 0.158 |
| PANSS negative | 0.088 | 0.062 | 0.158 | -0.035 | 0.212 |
| PANSS excitative | 0.417 | 0.163 | 0.012 | 0.093 | 0.741 |
| PANSS cognitive | -0.148 | 0.241 | 0.542 | -0.626 | 0.331 |

Explained variance for final model: \(R^2 = 0.354, F = 4.513, p < 0.05\).

| TABLE 3. Blockwise Multiple Regression Analysis of the Relationship Between Patient Characteristics and the CDSS Total Score Divided by Gender |
|---|---|---|---|---|---|
| Male \((n = 75)\) | B | Standard Error | Significance | Lower Bound | Upper Bound | Adjusted R Square |
| PAS childhood social | -0.034 | 0.269 | 0.900 | -0.572 | 0.504 |
| PAS childhood academic | 0.509 | 0.303 | 0.098 | -0.098 | 1.116 |
| PAS early adolescence social | 0.411 | 0.262 | 0.123 | -0.114 | 0.935 |
| PAS early adolescence academic | -0.054 | 0.548 | 0.922 | -1.150 | 1.043 |
| DUP | -0.005 | 0.289 | 0.986 | -0.584 | 0.574 |
| AUDIT | 0.189 | 0.060 | 0.003 | 0.069 | 0.308 |
| PANSS excitative component | 0.197 | 0.194 | 0.313 | -0.191 | 0.585 |
| Female \((n = 44)\) | B | Standard Error | Significance | Lower Bound | Upper Bound | Adjusted R Square |
| PAS childhood social | 0.758 | 0.423 | 0.082 | -0.102 | 1.618 |
| PAS childhood academic | 0.105 | 0.424 | 0.806 | -0.758 | 0.967 |
| PAS early adolescence social | -0.688 | 0.469 | 0.152 | -1.643 | 0.266 |
| PAS early adolescence academic | 0.601 | 0.739 | 0.422 | -0.903 | 2.105 |
| DUP | 0.687 | 0.343 | 0.054 | -0.011 | 1.384 |
| AUDIT | 0.025 | 0.103 | 0.809 | -0.185 | 0.236 |
| PANSS excitative component | 0.575 | 0.270 | 0.040 | 0.027 | 1.123 |

Explained variance for final model: male; \(R^2 = 0.292, F = 3.534, p < 0.05\); female; \(R^2 = 0.475, F = 4.272, p < 0.05\).
and PANSS excitative symptoms explained a significant proportion of the variance.

When we subsequently carried out 2 parallel multiple hierarchical linear regression analyses for men and women separately, AUDIT had the only significant contribution for men and PANSS excitative symptoms had the only significant contribution for women (Table 3).

DISCUSSION

The main finding of the current study was that almost 50% of patients in their first year of treatment for a schizophrenia spectrum disorder had experienced one or more MDE, while 21% met the MDE criteria at time of inclusion. The latter finding is in line with other studies (Koren et al., 1993; Sim et al., 2004), while the levels are lower than found in studies using less stringent criteria for depression (Birchwood et al., 2000).

Contrary to our expectations there were no differences between patients with and without a lifetime MDE concerning demographic characteristics or clinical measures. An earlier study (Bottlender et al., 2000) found that depressed patients were more likely to be older, more frequently married but unemployed. This might be due to differences in study populations as the Bottlender study was not based solely on FEP patients, but first admitted patients.

The present study revealed gender differences, as women were 3 times more likely than men to have experienced a MDE before their FEP. Furthermore, the PANSS excitative symptoms explained much of the variance in current severity of depressive symptoms for women. This is in line with previous research, that women besides being depressed are characterized by irritability, hostility, inappropriate affect, and impulsivity (Leung and Chue, 2000). The present study also revealed a significant association between drinking habits in men and current severity of depressive symptoms. Problem drinking in FEP has previously been found to be more pronounced in men and connected to suicidal behavior (Verdoux et al., 1999). Both these latter findings could represent the presence of gender specific coping strategies as indicated elsewhere in the literature (Read, 2004).

Interestingly, the DUP was significantly correlated to the current severity of depressive symptoms for women, but not for men. It could be that the stress of a long DUP generates depressive symptoms per se, due to deteriorating functioning in several areas, as suggested by the strong correlation between premorbid adjustment and the CDSS scores. On the other hand, there is a possibility that women more often are (mis)diagnosed as suffering from depression instead of psychosis and that this in turn leads to both a delay in treatment and subsequently to both more depressive episodes and longer DUP.

There are, to our knowledge, no previous studies that have explored the relationship between depressive symptoms during FEP and premorbid functioning. We found that level of depression at start of treatment was significantly associated with poorer premorbid childhood social and academic functioning. Level of premorbid functioning has previously been associated with negative symptomatology and quality of life (MacBeth and Gumley, 2008). This is also in line with the idea of a disturbed developmental pathway to depression in psychosis (Birchwood, 2003). It is possible that potential risk factors, such as suboptimal environments, psychological trauma, or childhood abuse not only could have a reciprocal impact upon the proneness for developing depression but also on premorbid adjustment and subsequently on the development of psychosis (Read, 2004).

There are several limitations to the present study. The cross-sectional design makes it impossible to conclude regarding the direction of the associations between depression and course of illness. The retrospective diagnosis of earlier MDEs might be confounded by the patients’ ability to remember the details correctly. There are, as usual in FEP studies, relatively more men compared with women in the present study.

In conclusion depressive symptoms are frequent among FEP patients, and not only concurrent with, but also predating the FEP. Gender differences both in the prevalence of MDE and clinical factors associated with high levels of depression suggests different pathways to depression in the context of psychosis in men and women. This needs to be explored further since the implications might be a more gender-specific approach to treatment of this serious comorbid condition.

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