Predictors of unrecognised comorbid depression in patients with schizophrenia at Amanuel mental specialized hospital, Ethiopia: a cross-sectional study

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INTRODUCTION

Both schizophrenia and depression are the most overwhelming psychiatric illnesses that have substantial contribution to the global burden of disease.1-3 Besides, patients with schizophrenia (PWS) have an increased risk of developing depressive symptoms compared with the general population.4 During the course of their illness, majority of PWS show depressive symptoms5 and therefore, depressive symptoms are an important part of schizophrenia.6

PWS develop depressive symptoms anytime during the course of the illness that is, either in the prodrome of a new episode, concurrently with the acute episode or in the post-psychotic period.7 However, negative symptoms in schizophrenia that are similar to those in depression such as apathy, lack of emotion or poor social functioning reflect a decrease in the level of normal functions.8

In addition, extra-pyramidal side effects, developing in relation with antipsychotic drugs, complicate the diagnosis of depression among PWS.9 Therefore, the occurrence of depression in PWS complicates the diagnosis and treatment process.

Co-occurrence of depression in PWS also affects the prognosis of the disease. This further increases the risk of relapse, frequency and duration of hospitalisation, and decreases social and occupational functioning.10
expected lifespan of PWS could be reduced by an average of 10–15 years, and suicide is the leading cause of this premature death among PWS. More than half of PWS attempts suicide and 9%–13% completed suicide in their lifetime, which could be more complicated and severe with presence of depression. Furthermore, emerging depressive symptoms are associated with impairment in everyday functioning, poorer quality of life, substance abuse and weak response to pharmacological treatment. A review of previous studies reported that prevalence of comorbidity of depression among PWS is 7%–75%, but on average, depression is observed in one out of four patients. Depressed mood is commonly associated with first and acute psychotic episodes of PWS. However, one-third of PWS reported depressive symptoms several months after the remission of a psychotic episode, recently termed “post-psychotic depression”. Studies reported that 25% of PWS developed post-psychotic depression and more than 80% of patients with first episode psychosis did suffer from depressed mood. Moreover, reports from longitudinal studies indicate that depressive symptoms have found to be prevalent during all stages of schizophrenia.

Depressive symptoms in PWS could be associated with responses to psychological stress or deficits, undesired side-effects of antipsychotics medications, substance or drug abuse and other organic or physical illnesses. Furthermore, social isolation, loss, unemployment, financial difficulties, adverse life events and stigma are some of the factors that are associated with depression in schizophrenia.

Yet, depressive symptoms that occur in PWS are often overlooked, inadequately characterised and not consistently integrated into treatment. Therefore, recognising depressive symptoms or episodes in PWS may promote the pharmacological treatment of depressive episodes and thus prevent subsequent suicide attempts or suicide. Therefore, the aim of this study was to assess the magnitude of unrecognised comorbid depression and predicting factors among PWS.

The present study is among the first in our community to underscore the hypothesis that depression is an important clinical phenomenon in schizophrenia. The most striking finding of this study is that it alerts mental health professionals about the unrecognised depressive symptoms in PWS.

**METHODS**

**Ethics statement**

The Institutional Review Board of Hawassa University, College of Medicine and Health Sciences approved the study and written informed consent was received from all participants.

**Study design, area and period**

From 1 to 30 March 2019, an institution-based cross-sectional study was conducted at Amanuel mental specialized hospital (AMSH) in Addis Ababa, Ethiopia. The hospital is one of the oldest in Ethiopia, having been founded in 1930 E.C. during the Ethio-Italian war, and it is the country’s only mental hospital. Each year, approximately 46 520 patients with psychiatric disorders visit as outpatients, and approximately 160 patients are admitted to the ward each month. The hospital has over 300 beds and serves patients with all types of mental disorders. There are 13 outpatient departments (OPDs) at the hospital. The hospital also serves as a teaching facility and a research facility for mental health sciences.

**Population**

All PWS who had a follow-up visit at AMSH belonged to the source population. The study population consisted of 306 patients with schizophrenia.

**Table 1** Sociodemographic characteristics of patients that participate on study of predictors of unrecognised depression in PWS at AMSH, 2019

| S.No | Variable | Categories | Frequency | Percentage (%) |
|------|----------|------------|-----------|----------------|
| 1    | Age      | 18–27      | 60        | 20.0           |
|      |          | 28–37      | 116       | 38.7           |
|      |          | 38–47      | 82        | 27.3           |
|      |          | ≥48        | 42        | 14.0           |
| 2    | Sex      | Male       | 203       | 67.7           |
|      |          | Female     | 97        | 32.3           |
| 3    | Marital status | Single   | 179       | 59.7           |
|      |          | Married    | 92        | 30.7           |
|      |          | Divorced   | 29        | 9.6            |
| 4    | Religion | Muslim     | 99        | 33             |
|      |          | Orthodox   | 148       | 49.3           |
|      |          | Protestant | 46        | 15.3           |
|      |          | Others     | 7         | 2.3            |
| 5    | Educational status | Illiterate | 70        | 23.4           |
|      |          | 1–8th grade| 75        | 25             |
|      |          | 9–12th grade| 122       | 40.7           |
|      |          | College and above | 33 | 11 |
| 6    | Occupation | Employed | 62        | 20.7           |
|      |          | Unemployed | 238       | 79.3           |
| 7    | Average monthly income | ≤US$18.4 | 201       | 67             |
|      |          | ≥US$18.5   | 99        | 33             |
| 8    | Place of residence | Rural | 78        | 26             |
|      |          | Urban      | 222       | 74             |
| 9    | Living status | With family | 244       | 81.3           |
|      |          | Alone      | 56        | 18.7           |

AMSH, Amanuel mental specialised hospital; PWS, patients with schizophrenia.
of all sampled PWS who had a follow-up visit at AMSH during the study period and met the inclusion criteria.

**Inclusion and exclusion criteria**
PWS who were 18 years or older were included in the study. PWS who were experiencing severe acute psychotic episodes and were unable to communicate were, however, excluded from the study. Clinical Global Impression Severity (CGI-S) Scale with seven-point scale was used to assess the severity of the psychotic episode. The CGI-S scale ranges from 1 (normal) to 7 (among the most seriously ill). Patients with a CGI-S score of 6 or higher were excluded from the study. Patients who were on antidepressant medication were also excluded.

**Sample size determination and sampling technique**
Using the consecutive sampling technique, 300 PWS were chosen from the AMSH OPD. PWS who visited psychiatry OPD during the study period and met the inclusion

The table below presents the clinical characteristics of PWS at AMSH, 2019:

| Variable                                      | Categories                  | Frequency | Percentage (%) |
|-----------------------------------------------|-----------------------------|-----------|----------------|
| Duration of Illness                           | ≤12 months                  | 24        | 8              |
|                                               | 13–60 months                | 100       | 33.3           |
|                                               | ≥61 months                  | 176       | 58.7           |
| History of known chronic illness             | Yes                         | 39        | 13.0           |
|                                               | No                          | 260       | 86.7           |
| Family history of mental illness             | Yes                         | 76        | 25.3           |
|                                               | No                          | 224       | 74.7           |
| Episodes of illness                          | Continuous                  | 74        | 24.7           |
|                                               | Single episode              | 82        | 27.3           |
|                                               | 2–4 episode                 | 87        | 29             |
|                                               | 5 and above                 | 57        | 19             |
| Any substance use in the past 12 months      | Yes                         | 84        | 28.0           |
|                                               | No                          | 216       | 72.0           |
| Medication adherence                         | Adhered                     | 232       | 77.3           |
|                                               | Non-adhered                 | 68        | 22.7           |
| Social support                               | Poor                        | 161       | 53.7           |
|                                               | Moderate                    | 99        | 33.0           |
|                                               | Strong                      | 40        | 13.3           |
| Positive symptoms of schizophrenia           | Delusional symptoms         | Yes       | 90             |
|                                               |                             | No        | 210            |
|                                               | Hallucinatory symptoms      | Yes       | 99             |
|                                               |                             | No        | 201            |
|                                               | Disorganised speech or behaviour | Yes | 26 |
|                                               |                             | No        | 273            |
| Negative symptoms of schizophrenia           | Anhedonia                   | Yes       | 102            |
|                                               |                             | No        | 197            |
|                                               | Asocialia                   | Yes       | 84             |
|                                               |                             | No        | 216            |
|                                               | Loose of personal motivation| Yes       | 67             |
|                                               |                             | No        | 232            |
|                                               | Loose of verbal expression  | Yes       | 35             |
|                                               |                             | No        | 264            |
| Suicide behaviour                             | Yes                         | 91        | 30.3           |
|                                               | No                          | 209       | 69.7           |

AMSH, Amanuel mental specialized hospital; PWS, patients with schizophrenia.
criteria were enrolled until the final study sample size was reached.

Data collection tools and quality assurance
A structured questionnaire administered by an interviewer was used to collect data. The questionnaire is divided into six sections: part one includes questions about patients’ sociodemographic characteristics and related factors; part two includes questions about patient clinical characteristics; part three is about patient social support; part four is about medication adherence; part five is about patients’ suicidal behaviour and part six is about depression screening. Psychiatrists, psychiatry residents and senior or expert mental health professionals made patient diagnoses based on Diagnostic Statistical Manual for Mental Disorders-5 diagnostic criteria.

The Calgary Depression Scale for Schizophrenia (CDSS) was used to assess the change in the level and intensity of unrecognised depressive symptoms in schizophrenia. It consists of nine items scored on a Likert scale (0=absent, 1=mild, 2=moderate and 3=severe). The lowest possible score is 0 and the highest possible score is 27. A CDSS score of more than 6 points has been proposed to distinguish PWS with depression from those who do not.

The level of social support among PWS was measured using the three-item Oslo Social Support Scale, with scores ranging from 3 to 14. To assess medication adherence in PWS, a four-item questionnaire adapted from a previous study was used. The four items have a scoring scheme of ‘Yes’=0 and ‘No’=1. The items are added up to give a score from 0 to 4, with 1 being adhered and 2 being non-adhered.

To evaluate suicidal behaviour the Suicidal Behaviour Questionnaire Revised (SBQ-R) with four items was used. SBQ-R item 1 assesses lifetime suicidal ideation and attempt; item 2 evaluates the frequency of suicidal ideation over the previous 12 months; item 3 assesses the threat of suicidal behaviour and item 4 assesses self-reported likelihood of suicidal behaviour. With a score of 3–18 and a cut-off point of 8, the sensitivity was 80% and the specificity was 91% for the adult clinical population.

To ensure the tool’s consistency and understandability, an independent person translated the English version questionnaire into Amharic and then back into English. Language experts were brought in to help with the translation of the questionnaire. The information was gathered by psychiatry nurses who were overseen by expert mental health professionals. Data collectors and supervisors were both given training. Before the main study, a pre-test on 5% of the study sample size was conducted at AMSH among PWS in the psychiatric ward to identify potential problems with data collection instruments, as well as to check the consistency of the questionnaires and the performance of the data collectors. Aside from that, the data collectors were supervised daily, and the completed questionnaires were checked daily by the supervisors and principal investigator.

Data processing and analysis
Before beginning analysis, the collected data were checked, coded and entered into Epi-data V.3.1 to minimise errors during data entry; the data were then exported to SPSS V.20 for cleaning and analysis. The sociodemographic and clinical characteristics of the patients were analysed using descriptive statistics, that is, frequencies and percentages were calculated for categorical variables. For each independent variable, an independent bivariate logistic regression analysis was performed against the dependent variable or CDSS. Variables with a p value of <0.05 were considered as candidates for multiple logistic regression to determine the variables that independently predict depression in simple binary logistic regression analysis. The multivariate analysis results were presented as crude and adjusted ORs. In multivariate logistic regression analysis, a p value of <0.05 was declared statistically significant at the 95% CI. Finally, the study’s findings were summarised using tables, graphs and narrative descriptions.

Patients and public involvement
Patients and the public were not involved in this study, including the recruitment, data collection, analysis, interpretation and dissemination of the results.

RESULTS
Sociodemographic and clinical characteristic of participants
The study included 300 PWS. More than two-thirds (203, 67.7%) of the participants were men, and 116 (38.7%) participants were between the age of 28 and 37 years. The majority of the participants (179 (59.7%)) were single, 238 (79.3%) of the study participants were unemployed and 257 (85.7%) were living with their family (table 1).
### Table 3  Bivariate analyses of risk factors for unrecognized depression in PWS at AMSH, 2019

| Variables                  | Category  | Depression | COR | OR (95% CI) | P value |
|----------------------------|-----------|------------|-----|-------------|---------|
| Age                        | 18–27     | 39 (74.6%) | 21 (25.6%) | 1           |         |
|                            | 28–37     | 87 (75.0%) | 29 (25.0%) | 0.619 (0.315 to 1.218) | 0.165   |
|                            | 38–47     | 58 (70.4%) | 24 (29.6%) | 0.768 (0.377 to 1.567) | 0.469   |
|                            | ≥48       | 25 (59.5%) | 17 (40.5%) | 1.263 (0.560 to 2.847) | 0.574   |
| Sex                        | Male      | 135 (66.5%) | 68 (33.5%) | 1           |         |
|                            | Female    | 74 (33.3%) | 23 (66.7%) | 0.617 (0.356 to 1.071) | 0.086   |
| Marital status             | Single    | 127 (71.0%) | 52 (29.0%) | 1           |         |
|                            | Married   | 63 (68.4%) | 29 (31.6%) | 1.124 (0.652 to 1.940) | 0.674   |
|                            | Divorced  | 19 (65.5%) | 10 (34.5%) | 1.285 (0.560 to 2.951) | 0.554   |
| Educational status         | Illiterate | 52 (74.2%) | 18 (25.8%) | 0.368 (0.154 to 0.876) | 0.024   |
|                            | Primary   | 52 (69.3%) | 23 (30.7%) | 0.470 (0.203 to 1.089) | 0.078   |
|                            | Secondary | 88 (72.1%) | 34 (27.9%) | 0.411 (0.186 to 0.904) | 0.027   |
|                            | ≥College   | 17 (51.5%) | 16 (48.5%) | 1           |         |
| Occupational status        | Employed  | 39 (62.9%) | 23 (37.1%) | 1           |         |
|                            | Unemployed | 170 (71.2%) | 68 (28.8%) | 0.678 (0.377 to 1.220) | 0.195   |
| Area of residence          | Rural     | 51 (65.3%) | 27 (34.7%) | 1           |         |
|                            | Urban     | 158 (71.1%) | 64 (28.9%) | 0.765 (0.442 to 1.325) | 0.340   |
| Living status              | With family | 186 (72.3%) | 58 (23.7%) | 1           |         |
|                            | Alone     | 23 (41.1%) | 33 (58.9%) | 4.601 (2.504 to 8.456) | <0.001  |
| Duration of illness        | ≤12 months | 15 (62.5%) | 9 (37.5%) | 1           |         |
|                            | 13–60 months | 76 (76.0%) | 24 (24.0%) | 0.526 (0.205 to 1.354) | 0.183   |
|                            | ≥61 months | 118 (67.0%) | 58 (33.0%) | 0.819 (0.338 to 1.983) | 0.658   |
| Known chronic illness      | Yes       | 18 (46.1%) | 21 (53.9%) | 3.183 (1.602 to 6.325) | 0.001   |
|                            | No        | 191 (73.1%) | 70 (26.9%) | 1           |         |
| Family history of mental Illness | Yes | 50 (65.7%) | 26 (34.3%) | 1.272 (0.730 to 2.215) | 0.395   |
|                            | No        | 159 (70.9%) | 65 (29.1%) | 1           |         |
| Episodes of illness        | Continuous | 53 (71.6%) | 21 (28.4%) | 1           |         |
|                            | Single episode | 60 (73.1%) | 22 (28.9%) | 0.925 (0.458 to 1.869) | 0.829   |
|                            | 2–4 episode | 57 (65.5%) | 30 (34.5%) | 1.328 (0.679 to 2.600) | 0.407   |
|                            | 5 and above | 39 (68.4%) | 18 (31.6%) | 1.165 (0.548 to 2.474) | 0.691   |
| Substance use              | Yes       | 55 (65.4%) | 29 (34.5%) | 1.310 (0.765 to 2.242) | 0.325   |
|                            | No        | 154 (71.2%) | 62 (28.8%) | 1           |         |
| Social support             | Poor      | 101 (62.7%) | 60 (37.3%) | 2.801 (1.166 to 6.724) | 0.021   |
|                            | Moderate  | 75 (75.8%) | 24 (24.2%) | 1.509 (0.592 to 3.847) | 0.389   |
|                            | Strong    | 33 (82.5%) | 7 (17.5%) | 1           |         |
| Medication adherence       | Adhered   | 175 (75.4%) | 57 (24.6%) | 1           |         |
|                            | Non-adhered | 34 (50.0%) | 34 (50.0%) | 3.070 (1.751 to 5.383) | <0.001  |
| Hallucination              | Yes       | 58 (58.5%) | 41 (41.5%) | 2.135 (1.279 to 3.562) | 0.004   |
|                            | No        | 151 (75.1%) | 50 (24.9%) | 1           |         |
| Delusion                   | Yes       | 49 (54.4%) | 41 (45.6%) | 2.678 (1.588 to 4.515) | <0.001  |
|                            | No        | 160 (76.1%) | 50 (23.9%) | 1           |         |
| Disorganised speech        | Yes       | 9 (33.3%) | 18 (66.7%) | 5.479 (2.356 to 12.741) | <0.001  |
|                            | No        | 200 (73.2%) | 73 (26.8%) | 1           |         |

Continued
Clinical characteristic of study participants

Majority of all participants (176 (58.7%)) have had their illness for more than 5 years, and 84 (28%) have used at least one type of substance in the previous 12 months. Among the most common symptoms hallucination and anhedonia, which affect one-third of the participants 99 (33%) and 102 (34%), respectively. Approximately half of the study participants (161 (53.7%)) had a poor social support, and 91 (30.3%) had suicide behaviour (table 2).

Magnitude of comorbid depression among patients with schizophrenia

Among 300 PWS, 91 (30.3%) have unrecognised comorbid depression according to CDSS (figure 1).

Independent predictors of unrecognised depression

Educational status, living status, known history of chronic medical illness, level of social support, medication adherence, positive symptoms (hallucination, delusion and disorganised speech), negative symptoms (anhedonia, asocialia, loss of personal motivation and alogia) and suicide behaviour are among the many variables that run in bivariate logistic regression analyses and become candidates for multiple logistic regression analysis at p value <0.05 (table 3).

Finally, in multivariate logistic regression model, living alone (AOR=3.488, 95% CI=0.455 to 8.363), having poor (AOR=4.434, 95% CI=1.448 to 13.581) and moderate (AOR=4.447, 95% CI=1.299 to 15.221) social support, non-adherence to medication (AOR=3.815, 95% CI=1.702 to 8.551), presenting with current negative symptoms such as asocialia (AOR=4.327, 95% CI=1.980 to 9.455) and loss of personal motivation (AOR=3.462, 95% CI=1.528 to 7.844), and having suicidal behaviour (AOR=6.834, 95% CI=3.240 to 14.411) were the significant predictors of unrecognised comorbid depression among PWS as shown in table 4.

DISCUSSION

The primary aim of this study was to determine the prevalence of unrecognised comorbid depression among PWS. This study found out that nearly one-third of PWS (30.3%) has undiagnosed depression in a stable phase of the disease. This is in agreement with previous studies 30% in Egypt, 27.2% in Greece and 31% in Spain. Similarly, a study among PWS living in a nursing home found out that more than one-fourth (26.5%) were present with depression. However, higher prevalence (56%) of depression was reported by Cardoso and his colleagues based on the CDSS among PWS. In addition, the prevalence of comorbid depressive symptoms was reported to be 40.6%–54.6% in patients with Chinese chronic schizophrenia which is higher than our finding. This inconsistency might be explained by the fact that previous studies may have included some patients in the acute phase because the higher rate of depression is reported in the prodromal and acute phases compared with the stable phase of schizophrenia. Similarly, in this study, patients treated with antidepressants were excluding from the study too.

With respect to our overall theoretical model, we found that 13 categories of variables were significant in bivariate analysis and that only seven retained statistically significance in multiple logistic regression analysis. Patients who were living alone, having poor and moderate social support, non-adherence to medication presenting with current negative symptoms like asocialia and loss of personal motivation and suicidal behaviour were identified as a number of variables that were associated with higher rates of unrecognised comorbid depression in people with schizophrenia.

Our study found out that depression rate of PWS who were living alone and had poor or moderate social support was quite higher as compared with their counterparts. This indicates that lack of family support and environmental conditions like having inadequate social support
could be important factors in the exhibition of depressive symptoms in PWS. In addition, social support is postulated to safeguard mental health through the benefits of social relationships and as a buffer against stressful conditions. Therefore, support from a spouse, relatives or friends is supposed to have independent protective effects against depression.

Our results, consistent with the literature, found an association between having chronic physical illnesses and depression. In our study, patients with any type of chronic illnesses like diabetes, HIV/AIDS, cancer, hypertension and so on have two times more likely to have depression than those without chronic illnesses. Moreover, the interplay among physical illness and depression in PWS is probably bidirectional. Living with depression and a chronic physical illness can make life more complicated. It can make living harder to find the energy to work, exercise, interact with family members and friends or take medication regularly. This could make you feel isolated and make it firmer to get better from depression easily.

This study showed that people with schizophrenia who are non-adherent to their anti-psychotic medication were nearly four times at higher risk to develop depression.
is fact that patients who are adherent well to their treatment had decreased symptomatology and become functionally and occupationally. This reduces stigma, increases self-esteem, and inspires hope in PWS, which indirectly reduces the risk of depression. Studies reported that depression could occur in antipsychotic-free PWS and the magnitude of significant depression decreases when antipsychotic treatment is started. In fact, several studies found out that antipsychotic medications do not seem to induce depressive syndromes in PWS. On the other hand, other reports tend to underline that neuroleptic medications are responsible for the development of depressive episodes in PWS.

In our study, patients with negative symptoms that is, those who had asocialia and loss of personal motivation were more than four and three times greater risk of developing depression, respectively. This could be due to the fact that the conceptual overlap between depressive syndromes and negative symptoms. Furthermore, antipsychotic medications could have aetiological role in depressive symptomatology in schizophrenia associated with its action on dopaminergic pathways (play major role in reward and pleasure) and extra pyramidal side-effect that causes ‘akinetik depression’. There is no clear boundary between the two syndromes. However, it is fact that the presentations of the symptoms are different qualitatively and subjectively in the context of depression and negative symptoms.

Those PWS having suicidal behaviour were nearly seven times more likely to have depressive features. Similar to our finding, Gokhan et al. found statistically significant higher CDSS average score in patients with suicidal ideations and wishes as compared with their counterparts. Nearly 10% of people with schizophrenia commit suicide, and most of them had history of depressive episodes or had presented with signs or symptoms of depression during their contacts with health workers.

Even though, this study provided a baseline data, and we use a standardised tool (CDSS) designed to assess depression in PWS, it also has some limitations encountered. Exclusion of patients who were on antidepres- sants medications and studying only PWS in outpatients could have led to an underestimation of the prevalence of depression. Our study was a cross-sectional design that does not show cause and effect relationship also might be considered as limitation. It might be difficult to generalise the findings of this study due to the reason that this study was conducted using non-probability consecutive sampling method and small sample size. In addition, even though, we use internationally validated instrument to assess depression, CDSS was not yet validated in Ethiopia.

CONCLUSION AND RECOMMENDATIONS

Nearly one-third of PWS have undiagnosed depression in a stable phase of the disease. Therefore, the prevalence of unrecognised depression in this study was found to be 30.3%. The likelihood of having unrecognised comorbid depression was higher among those living alone, and those having poor and moderate social support. Furthermore, non-adherence to medication, presenting with negative symptoms like asocialia and loss of personal motivation, and having suicidal behaviour were significantly associated with comorbid depression.

Therefore, we recommend clinicians better to strengthen early screening of comorbid depression among PWS and take early appropriate treatment measures in order to prevent or lessen the burden of depression on the treatment outcome of schizophrenia. Our key recommendation to psychiatrists and mental health professionals who treat PWS and depression is to perform a careful diagnostic assessment, which is essential to tailor appropriate treatments. From our results, we have firm grounds that those clinicians to initiate suitable psychosocial interventions and medications for PWS.
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