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Long-term clinical course and outcome of schizophrenia in rural Ethiopia: 10-year follow-up of a population-based cohort

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ABSTRACT

Background: Although the few available studies from LMICs report favorable outcome, the course of schizophrenia is more complex than has been indicated so far.
Methods: A sample of 361 people with a standardized clinical diagnosis of schizophrenia were recruited from a predominantly rural community in Ethiopia and followed up regularly for an average of 10 years. Psychiatrists used the Longitudinal Interval Follow-up Evaluation chart to carry out assessment of illness course. Duration of time in clinical remission was the primary outcome.
Result: About 61.0% of the patients remained under active follow-up, while 18.1% (n = 65) were deceased. The mean percentage of follow-up time in complete remission was 28.4% (SD = 33.0). Female patients were significantly more likely to have episodic illness course with no inter-episode residual or negative symptoms ($\chi^2 = 6.28$, P = 0.012). Nearly 14.0% had continuous psychotic symptoms for over 75% of their follow-up time. Only 18.1% achieved complete remission for over 75% of their follow-up time. Later onset of illness was the only significant predictor of achieving full remission for over 50% of follow-up time in a fully adjusted model. Conventional antipsychotic medications were fairly well tolerated in 80% of the patients and 4.2% (n = 15) experienced tardive dyskinesia.
Conclusion: This population-based study is one of the very few long-term outcome studies of schizophrenia in LMICs. The study demonstrated clearly a differential and more favorable course and outcome for female patients but overall course and outcome of schizophrenia appeared less favorable in this setting than has been reported from other LMICs.

1. Introduction

Prospective population-based studies of course and outcome of schizophrenia are scarce in low and middle-income countries (LMICs) (Thara and Rajkumar, 1992; Ohaeri, 1993; Thara et.al., 1994; Gureje and Cohen, 2011; Novick et al., 2012). Nevertheless, the clinical and functional course of schizophrenia in LMIC settings is presumed to be favorable (Sartorius et al., 1978).

This discourse of a more favorable outcome in LMICs appears to have first emerged in reports from Africa (Murphy and Raman, 1971). Subsequent data from the World Health Organization (WHO) multi-country studies (the International Pilot Study of Schizophrenia—IPSS—and the Determinants of Severe Mental Disorders—DOSMD) supported the initial reports (Sartorius et al., 1977; Sartorius et al., 1978; Jablenisky et al., 1992). Both the IPSS and DOSMD involved a single country, Nigeria, from Africa. In the IPSS-Nigeria study (Sartorius et al., 1977), 42.6% (n = 60/141) had a diagnosis other than schizophrenia. Participants with a diagnosis of schizophrenia had either paranoid or catatonic schizophrenia. In the DOSMD-Nigeria sample (Jablensky et al., 1992), nearly 20% (n = 26/142) did not receive the core diagnosis of schizophrenia and 76% of the participants were married. The cohort also had one of the highest proportions of participants in receipt of treatment despite a 31% drop out rate. The Nigerian cohort had the best short term outcome in both the IPSS and DOSMD. However, this outcome has to be seen in the context of the atypical nature of the sample.

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Since these earlier reports, the notion of better outcome in LMICs has persisted (Kulhara et al., 2009; Novick et al., 2012). The counter-intuitive nature of the evidence has been a point of contention given the high mortality (Ran et al., 2007), and other poor prognostic factors (Sartorius et al., 1978; Sartorius and Janca, 1996; Mojtabai et al., 2001; Kurihara et al., 2006; Cohen et al., 2008), including poor access to treatment and long duration of untreated psychosis (DUP) (Shibre et al., 2003; Farooq et al., 2009), which in turn predisposes to poorer outcomes (Perkins et al., 2005; Kurihara et al., 2006; Ran et al., 2007; Crumlish et al., 2009; Farooq et al., 2009; Teferra et al., 2011). Other factors such as internalized and public stigma (Shibre et al., 2002a,b; Van Zelst, 2009; Assefa et al., 2012), absence of formalized social safety nets leading to over-burdened caregivers (Shibre et al., 2003), and environmental factors are all likely to contribute to poorer outcome in LMICs.

The most recent series of reports on the outcome of schizophrenia come from the Butajira cohort in Ethiopia (Kebede et al., 2005; Alem et al., 2009; Teferra et al., 2011).

These reports focused on short-term outcomes, which are likely to exaggerate negative outcomes. Therefore, we followed-up patients for additional years to provide evidence on the longer-term outcome of schizophrenia in LMICs. This data extends the evidence on the outcome of schizophrenia in LMICs. First, this is the largest single site study of the outcome of schizophrenia in Africa and, to our knowledge, any other LMIC. Secondly, patients were serially monitored with rich clinical data throughout the course of follow-up. Third, a more complete data was obtained on all subjects at the time of final follow-up. Fourth, participants were recruited from the population and are potentially the first population-based cohort from any LMIC and are likely to be a more true representation of the course of illness. Finally, the duration of follow-up was relatively long, offering a more realistic evidence on the course of schizophrenia.

2. Methods

The details of the case identification methods for the Butajira cohort have been reported previously (Shibre et al., 2002a,b; Kebede et al., 2003; Kebede et al, 2004; Fekadu et al., 2006; Alem et al., 2009) and are outlined briefly below.

2.1. Study participants

The recruitment of participants took place between March 1998 and May 2001 and followed a two-stage method. In the first stage, 68,378 adults aged 15–49 years were interviewed through a house-to-house survey using the Composite International Diagnostic Interview (CIDI 2.1) (Sartorius and Janca, 1996; Ustün et al., 1997), augmented by the Butajira key informant method (Shibre et al., 2002a,b). For those who screened positive in the first stage, diagnostic assessment was conducted using Schedules for Clinical Assessment in Neuropsychiatry (SCAN 2.1) (Sartorius and Janca, 1996; Ustün et al., 1997). Following the SCAN interview, 321 cases (at initial enrollment) and 40 incident cases (through leakage survey) with confirmed schizophrenia (APA, 1994; World Health Organization, 1994), were recruited into the cohort. Thus 361 participants were followed up for a mean follow-up period of 10 years (range: 1–156 months), (Fig. 1.). All patients had access to basic psychiatric treatment, mainly first generation antipsychotics (haloperidol, chlorpromazine, thioridazine and fluphenazine decanoate) and tricyclic antidepressants (amitriptyline and imipramine), which are also commonly used in other psychiatric clinics in the country. Doses of antipsychotic medications, in chlorpromazine equivalent doses (Taylor et al., 2009), were between 25 mg and 300 mg/day. Tolerability of antipsychotic medications was assessed clinically as part of the final review.

Clinical follow-ups were carried out monthly at the Butajira psychiatric clinic and two outreach clinics established by the research project. At each visit, any complaints, pertinent findings from a mental state examination, overall clinical impression and treatments were recorded. All patients with established diagnoses of schizophrenia who had at least one follow-up assessment after enrollment were included in the analysis.

2.2. Instruments

The following instruments were completed for all patients annually; Basic Information on the Study Subjects and informants, Scales for Assessment of Negative Symptoms (SANS) (Andreason, 1982; Andreasen, 1984), Scales for Assessment of Positive Symptoms (SAPS) (Andreasen, 1984), Life Chart Schedule (LCS) (Sartorius and Janca, 1996), Mania Rating Scale (MRS) (Young et al., 1978) and the Hamilton Rating Scale for Depression (HRSD) (Hamilton, 1960). The following forms were completed as indicated: refusers and deceased patients form, Broad Rating Scale (BRS) (Sartorius and Janca, 1996) and physician reviewed verbal autopsy questionnaires (Soleman et al., 2006; Abbas et al., 2011). The mean carer-burden score and carer-perceived stigma score at baseline were computed from the Family Interview Schedule (FIS) (Sartorius and Janca, 1996). A comprehensive physical examination, assessment for involuntary muscle movements and neurological soft signs were carried out at enrollment (Shibre et al., 2002b).

Course and outcome data was collected using the Longitudinal Interval Follow-up Evaluation (LIFE) chart (Keller et al., 1987). LIFE chart is a semi-structured questionnaire suitable for summarizing longitudinal data. Four psychiatrists who were trained for four days administered the LIFE chart. Training was conducted by a trainer (AF) who was trained by the developers of the LIFE chart methodology in the USA. The Ethiopia training included formal presentations by the trainer, ratings of recorded training video interviews, and pilot interviews in selected community samples around Butajira. The LIFE chart has been in use for over four decades and validated for use in different settings and for gathering longitudinal clinical data in psychiatric illnesses (Warshaw et al., 2001; Judd et al., 2005). Although it was initially designed to assess the longitudinal course of affective symptoms, utility of the LIFE chart for rating the course of any psychiatric disorder is accepted (Keller et al., 1987) and has been used in LMIC (Shibre et al., 2014). The key rating tool in the LIFE chart is the Psychiatric Status Rating (PSR). The PSR is a six-point symptom severity rating, ranging from one to six. A rating of one indicates the absence of symptoms while a rating of six is consistent with severe symptoms. The PSR ratings allow calculation of mean scores or categorization of these symptom severity ratings into three threshold categories. Thus, a score of one and two were indicative of remission; a score of three and four were indicative of partial remission or a sub-threshold state, and a score of five and six were indicative of the occurrence of a full syndromal episode as defined in the DSM-IV. For alcohol and khat abuse or dependence, a three-point scale, corresponding to the three threshold categories, remission, partial remission or sub-threshold state and episode, was used. The PSR ratings were completed using all available information: reports by patients and family, the monthly clinical records, annual symptomatic and functional ratings, reports from psychiatric nurses, and reports from the project outreach workers who had monthly contacts with the patients and their families. When patients were unable to attend the psychiatric clinic for the final assessment, raters visited the patients' house with their permission. Two consultant psychiatrists trained in the use of the LIFE chart (AF and TS) supervised the ratings. Data on reliability of the PSR scores, medication tolerability and extrapyramidal side effects (EPS) of medication were all scored using items in the LIFE-chart. Level of functional impairment was measured using Global Assessment of Functioning (GAF).

2.3. Outcome measures

The primary outcome was the duration of follow-up in a state of remission, expressed in terms of percentage of the follow-up time