Twenty-five years of schizophrenia: The Madras longitudinal study

Thara Rangaswamy
Director of Schizophrenia Research Foundation, Chennai, Tamil Nadu, India

ABSTRACT

Aim: To determine the 25 year follow-up of subjects originally enrolled in the “Study of factors associated with course and outcome of schizophrenia” (SOFACOS) at Chennai.

Materials and Methods: All subjects who were followed up were administered the same research tools which were done at inclusion, namely the PSE & PPHS.

Results: At the end of 25 years, 47 of the original ninety subjects were assessed completely. Twenty five (26%) had died and 18 (20%) were lost to follow-up during the 25 year period. 32 of the 47 followed up were in partial or total remission. Outcome was good in 27.7%, intermediate in 52% and poor in 19%. More men were single and more women were either married or separated. Gender differences were not marked.

Conclusions: This is one of the few prospective, long term follow up studies from India. Although outcome was good in those followed up, the numbers who died and could not be followed up causes concern.

Key words: First episode, schizophrenia, follow up, course and outcome

INTRODUCTION

Although course and outcome of schizophrenia has been a subject of keen interest ever since Bleuler’s first account of his patients, the advent of the second generation drugs has further enhanced this interest. Long-term follow-up studies (over 20 years of follow-up) have however been few and far between and have largely been European or American in origin. Comparison of outcome in various countries/ cultures was first done in the international pilot study of schizophrenia (IPSS)\(^1\) and more recently the International Study of Schizophrenia, \(^2\) a follow-up study of the cohorts of the earlier world health organization (WHO) studies also addressed this issue.

There have been very few long-term follow-up studies of schizophrenia from India except for the sites that formed part of the WHO studies. This paper is on the 25-year follow-up of the Madras Longitudinal study. It describes the course of illness, symptom profile and occupational functioning after 25 years of illness. Earlier publications have dealt with outcome and other aspects at various points in time.\(^{3,4}\)

MATERIALS AND METHODS

The original study called the “Factors affecting course and outcome of schizophrenia” included in the Chennai center 90 first episode patients who fulfilled international classification of diseases-9\(^{th}\) version criteria for schizophrenia. While follow-up was rather rigorous for the first 10 years, subsequent follow-up occurred after 15, 20 and 25 years owing to lack of funding.

Study site

The original site was the Department of Psychiatry, Madras Medical College where inclusion and follow-up for the first 5 years was completed. Further follow-up was done at the Schizophrenia Research Foundation, an NGO dealing with...
care and research. The 10-year data was analysed at the Johns Hopkins Institute, USA, as part of a collaborative venture. The sample was also included in the international study of schizophrenia (ISOS) study coordinated by the WHO.

**Instruments**
Informed consent was obtained from all patients and their families. The following instruments were administered on patients and carers.
1. The present state examination (PSE-9). Since this had been used at inclusion, it was also used at the end of 25 years. The PSE scores were grouped into 33 syndromes that were used in the analysis.
2. The Psychiatric and Personal History Schedule has an inclusion and follow-up version. This elicits demographic and historical variables.
3. Detailed interviews with subjects and their care givers as well as case notes whenever available. The author carried out all the assessments at the end of 25 years.

**RESULTS**

**Features at inclusion**
The sample of 90 first episode schizophrenia patients was largely urban and had an equal gender distribution; (Each 45) which happened by chance and not by design. The age ranged from 17 to 38 years with a mean of 24.5. The age of onset did not differ in the two sexes. The mean number of years of education was about 11 years. Most were from middle and lower socioeconomic groups and all of them lived with their families, of which 79% were nuclear and the rest joint and extended. About 60% of the sample was single, and 69% had their onset of illness before 24 years. Onset was insidious in over half the sample.

**At the end of 25 years**
Of the original 90, 25 (26%) had died, 18 (20%) were lost to follow-up and 47 (53%) were assessed completely. Of those who could not be traced, 10 had moved outside the city, two had wandered away and could not be traced and six had moved without leaving any new address behind. Two families of women patients did not want us to contact the patient since they were now married and the husbands and their families had not been informed about the illness. Although some information was available on these two subjects, they were treated as drop-outs since complete assessments could not be done.

Two patients were in hospital for a prolonged period- one was in the Institute of Mental health and the other in SCARF. Twenty-five patients had died during this period (14 males). Of these, eight had committed suicide (4 males). Although the others were due to illness, in some cases it was not possible to ascertain the exact cause of death due to lack of medical records. Of the 25 deaths, 12 happened in the first 10 years of follow-up.

**Clinical picture**
PSE was administered to all these patients. At the time of assessments, 32/47 (16 of each sex), were in partial or total remission, 10 were in a relapse episode and 5 were continuously ill. Since the follow-up after 10 years was not regular, it was not possible to assess the exact duration of the relapses in all cases.

Most symptoms had shown a decline since years 10 and 20. Since 10 patients were in relapse episode, positive symptoms were recorded in them. Formal thought disorder and hallucinations were present in seven, and delusions, mostly of persecution and reference in 10 patients. Depression was seen only in eight while slowness and blunted affect was seen in 27 and 17, respectively.

It is interesting that even after 25 years, 15 patients did not have complete insight into their condition. Five totally denied illness and treatment, while the others had partial insight to the extent they knew it was a health related problem, but had difficulty in acknowledging it as a psychiatric disorder.

**Pattern of course**
Seven patients had recovered completely. They did not have any episodes after the first one and were functioning well. Another four also did not have any more episodes, but had mild residual features. As expected, most (31/47) have had multiple relapses with varying degrees of remission between episodes. Only five patients were continuously ill during entire 25-year period [Figure 1].

**Treatment**
At the end of 25 years, 20/47 were not taking any kind of medication. Of these 20, 16 patients or families felt that they had improved considerably and did not need medication. One patient was wandering and hence remained untreated. Two stopped medication and switched over to other alternative forms (Homeopathy, Ayurveda) since they felt they were not improving.

| Description of pattern                        | Frequency | % |
|-----------------------------------------------|-----------|---|
| Complete recovery without relapse             | 7         | 15 |
| No relapses, but with residual symptoms       | 4         | 08 |
| One or more relapses, complete remissions     | 14        | 30 |
| One or more relapses, incomplete remissions   | 17        | 36 |
| Continuously psychotic                        | 5         | 11 |

[Figure 1: Patterns of course]
Twenty were on typical antipsychotics, 4 on atypicals and 3 on a combination of both. Six patients received antidepressants and two mood stabilizers. Sixteen of the 20 continued treatment at SCARF, while 4 had switched over to the Institute of Mental Health, Chennai.

Two were long-term in-patients, one in SCARF and the other in institute of mental health, Chennai. These admissions were necessitated by poor drug compliance and social reasons. It is significant that in the 25-year period, only 12 patients were hospitalized. Most of the treatment was on an out-patient basis.

Pattern of course
Right from the beginning of this study, five course patterns were described. They were complete remission, remission with residual features, multiple relapses with complete remission, multiple relapses with incomplete remission and continuous illness. Graph 1 details the number of patients in each group.

Outcome was good in 13 (27.7%), poor in 9 (19%), intermediate in 25, (52%). No gender differences in outcome were observed.

The good and poor outcome groups were compared using univariate analyses. The following variables were significantly more in the poor outcome group. They were:

- Being in a relapse at 25 years ($P<0.000$), unfavorable pattern of course of illness ($P<0.000$), greater number of suicide attempts ($P<0.004$), socioeconomic problems ($P<0.015$), presence of dangerous behavior ($P<0.000$), being unemployed ($P<0.001$) and presence of formal thought disorder, hallucinations, delusions, apathy, and blunted affect.

Employment
Of the 24 males, 13 were unemployed, 11 were gainfully employed and supporting themselves and their families. Six women held jobs.

Marital status
More women than men were both married and separated/divorced. Of 30 who remained married at the end of 25 years, 18 were women, of the 6 divorced, 4 were women. However, more men remained single (8/11).

Sources of support
Nearly 32% of the sample supported themselves financially, while in 36% it was the spouse, 17% parents, and the rest by others such as uncles, in-laws, etc.

DISCUSSION
This long-term follow-up is one of the few from India and developing countries. Longitudinal assessment of clinical processes such as symptom profile, course and outcome as well as variables related to functioning like job/work and employment and marriage have been possible. The follow-up rate after 25 years (excluding deaths) in Madras longitudinal study is 47% and 80% if the deaths are included. This is indeed very impressive considering there are no movement registers in our country and it is impossible to keep a tab on internal migration unless notified by the family. This rate also compares favorably with other ISOS centers with a similar period of follow-up [Table 1].

The process of follow-up was fraught with difficulties in two kinds of patients. Those who had improved and were stable were reluctant to be interviewed periodically and wanted to be left alone. The other group was an all female group comprising of those who had married after the onset of the study and had not disclosed all details of their illness to the husband and his family. In some of these cases, the interviews had to be done only when the patients visited their parental homes.

It can be seen that the follow-up rate was much higher in the early years of follow-up (upto 10 years) and gradually declined after that. One reason for this could be that the study was funded by external sources in the first 10 years which made it possible to have a rigorous follow-up. After that, the staffing declined and it was difficult to maintain the same rigor without funding. It is also likely that patients report regularly for follow-up during the early course of their illness and as years roll by, their regularity also comes down, specially if many of them have attained partial or total remission.

Unlike the observation in some studies, [7,8] sex differences were unremarkable in this cohort. It was, however, noted that more women were separated or divorced while more men remained single. However, the symptoms, course and outcome were all similar.

Since outcome has been measured in a multi-dimensional fashion, it is no surprise that a combination of clinical and sociodemographic variables have differentiated between good and poor outcome.

Nearly 50% of the sample has discontinued medication. This again is not surprising considering the chronic nature of the illness and the long period of follow-up of 25 years. What is however gratifying is that 80% of those who discontinued

| Table 1: Comparison of follow-up details among centers |
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| **Center** | **Fup** | **Sample** | **Intake** | **Deaths** | **Lost %** | **Fup %** |
| Cali | 26 | Clinic | 101 | 12 | 17 | 71 |
| Agra | 26 | Clinic | 140 | 31 | 26 | 43 |
| Prague | 26 | Clinic | 125 | 37 | 29 | 34 |
| Chennai | 25 | Clinic | 90 | 27 | 19 | 47 |
medication were in varying states of remission and it was felt by the treating team that only 4 of those who discontinued should have been on medication.

Rates of hospitalization during the entire follow-up period were low. This may not truly reflect just the severity of the illness, but the resources in terms of hospital beds available. In many developing countries including India, hospitalization alone cannot be considered as an indicator of the severity of the episode, be it at inclusion or a relapse. Further since admission into a mental health facility carries a lot of stigma, many families prefer to care for their ill members at home itself even if it at the expense of disruption of family life and routines.

There is a lot of on going discussion on what constitutes remission and recovery and who decides this. It is being increasingly felt by persons with serious mental illness that they would like to reclaim their lives without first being cured of mental illness. This is also what is seen in the lives of many patients who are able to function to varying extents despite the presence of active hallucinations or delusions.

Some of the patients have improved significantly. This is not an unknown feature of schizophrenia, and Kendell in his commentary remarks that improvements can occur even after many years.

The sample has had a predictable pattern of course with most persons having had one or more relapses. The episodic course in schizophrenia has been observed in many long-term follow-up studies such as the 26-year longitudinal study by Harrow. The author also draws attention to the fact that a subgroup of schizophrenia patients who a few years after the acute phase are able to show remission of symptoms and function adequately even without treatment.

Only 5 were ill throughout the 25-year period. The outcomes have been satisfactory and comparable to the outcomes of this cohort at the end of 10 and 20 years. It is also not very different from that reported from developing countries in the ISOS study. However, considered the rather high mortality rate of the sample and the lack of information on drop outs, we cannot be categorical in stating that the outcome of the entire sample has been good.

The high rates of marriage in this sample has been a fairly consistent finding. An earlier publication on the 10-year follow-up of this cohort also found a high rate of 70% with more men being single. The trend seems to continue over time.

The other fact that needs to be borne in mind is that this was a closely followed up cohort, at least in the first 10 years which also ensured to an extent adherence with medication and good psychosocial support. This could well be one of the factors influencing a better outcome. The fact that all but two of the patients live with their families even at the end of 25 years of a chronic illness and are supported by them is indeed heartening and speaks volumes of the resilience in Indian families.

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