



Outcome Determinants and Parameters in Late-Life Schizophrenia

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Introduction

Schizophrenia is a complex disorder of thought, perception, cognition, emotion, and behavior which usually manifests in the second or third decade of life [1]. However, it is not uncommon for the disease to have an onset in extremes of age, i.e., childhood as well as old age [2, 3], and has even been described in a 100-year-old individual [4]. Eugen Bleuler's son, Manfred Bleuler, demonstrated that schizophrenia can manifest for the first time in later life and even suggested a clinical subdivision based on age at onset [5, 6]. Though Kraepelin initially conceptualized schizophrenia as “dementia praecox” in order to suggest that this disorder had a dementia-like pattern, but which emerged earlier, later on he found that some of the older people may develop schizophrenia for the first time during old age [1].

Concept, Types of Presentation, and Classification

Schizophrenia in the elderly tends to present in different manners:

- (a) Schizophrenia is generally diagnosed quite early in the individual who then continues to live with the disorder through middle age and subsequently old age [7]. These are the older people with schizophrenia having an onset before the age of 40 years, the so-called early-onset schizophrenia (EOS) [8].
- (b) Individuals who have onset of schizophrenia after the age of 40 years. As per the consensus statement by the International Late-Onset Schizophrenia Group, these individuals with schizophrenia should be called as “late-onset schizophrenia (LOS)” [1].
- (c) Lastly, a group of people in whom schizophrenia-like psychosis may be present for the first time with onset after age 60 years. This group has been labeled as “very-late-onset schizophrenia-like psychosis (VLOSLP)” [1].

It needs to be borne in mind that the term “late-life schizophrenia” is usually used for all older persons with schizophrenia without taking into consideration whether it is EOS, LOS, or VLOSLP; but principally it more often than not includes the first two entities [5].

However, it needs to be mentioned here that a clear delineation of schizophrenia as per onset of age is neither included nor emphasized in the most recent (DSM-IV) or current (DSM-5 or ICD-10) classificatory systems. Only DSM-III-R classificatory system mentioned LOS as those who had onset of symptoms after the age of 44 years, and it

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is seen that about 15–20% of all patients with schizophrenia fall in this category [7].

Schizophrenia in the elderly also needs to be differentiated from “paraphrenia,” a late-onset delusional disorder in the elderly with prominent persecutory delusions without any association with dementia [9]. It should be noted that delusional disorder in the elderly has often been referred to as paranoia, paranoid reaction, paraphrenia, paranoid psychosis, paranoid condition, paranoid state, and paranoid disorder [5]. Unfortunately, it has been observed that this only generates more ambiguity, and hence the usage of the term “paraphrenia” is best avoided for any particular entity.

All throughout this text, only EOS and LOS will be discussed, mostly because they are the ones which can be considered as “late-life schizophrenia” in the true sense. Both EOS and LOS have some similarities as well as some differences.

Similarities Between EOS and LOS

- (a) Positive symptoms are present in both [1].
- (b) 10–15% may have a family history of schizophrenia [1].
- (c) History of clinical maladjustments is present in both groups [1].
- (d) Both show response to antipsychotics, though dosages used may differ [1, 11].
- (e) Cognitive dysfunction is prevalent in both groups [7].
- (f) Neuroanatomical findings on CT scan and MRI reveal enlargement of lateral and third ventricles (suggesting tissue loss) in both groups [7]; focal structural changes are present in both groups [5].
- (g) Both have a chronic course and similar severity of global psychopathology [5].
- (h) Both have two to three times greater mortality rates in comparison to various groups [5].
- (b) Phenomenology: There is relative absence of thought disorder in LOS. Affective blunting is absent or found in lesser degree compared to EOS [12, 13]. LOS may have partition delusion (the belief that people, animals, objects, or radiation can pass through structures that in usual circumstances would have been a barrier to such passage) [14], persecutory delusions [14, 15], and phantom boarder (that guests are living in the person’s house when actually no one was there) [5]. Studies have reported that LOS have less severe negative symptoms, though evidence to the contrary also exists [5]. Presence of paranoid symptomatology is more common in LOS [5, 10]. Visual, tactile, and olfactory hallucinations are present with greater frequency in LOS individuals in comparison to those with EOS [5].
- (c) Cognition: LOS individuals were better than EOS when abstraction/flexibility of thinking, semantic memory, and speed of processing were considered [5]. On the other hand, EOS individuals had less impairment on auditory and visual attention compared to those with LOS [16].
- (d) Functioning: LOS individuals were found to have better premorbid functioning than those having EOS [10] when their socio-occupational history was considered [17, 18], and LOS individuals were likely to have been married at some point in time [5]. When the daily functioning as well as health-related quality of life was assessed, it was found that LOS individuals fared better than those with EOS [19].

Outcome Parameters

To track the course and outcome parameters of late-life schizophrenia is very challenging. This is due to innumerable reasons like:

Differences Between EOS and LOS

- (a) Gender: LOS has a preponderance for the female gender, a finding which has been consistently reported [5, 10, 11].
- (a) There are hardly any follow-up studies [20].
- (b) Even when studies are present, findings may vary depending upon the methodology used like the nature of sample selected, whether there is presence of comorbid con-

ditions (which are often present in elderly), age at which psychotic symptoms first appeared, etc. [8].

- (c) Defining the exact age at onset itself might be challenging, as this information is often gathered from the elderly patient or from his caregivers who are also his contemporaries; thus the information could be inaccurate, as it will be based on recall which may be compromised due to potential cognitive impairment in the elderly [3].
- (d) Follow-up of LOS patients is arduous due to limited social support of these patients, comorbid medical conditions that may interfere with treatment follow-up, presence of sensory deficits which may limit patient's mobility, and various other factors [3].
- (e) Presence of ethical considerations for this vulnerable group may restrict the investigators to exclude the elderly from research.
- (f) Symptoms of psychosis in the elderly may often be attributed to organicity or due to age-related changes.

Despite these abovementioned limitations, various reviews and studies have been able to throw some light on the course and outcome of late-life schizophrenia.

Risk Factors

Despite some confusion, many studies and reviews have hinted at some of the risk factors for late-onset psychosis. These are:

- (a) Sensory deficit, especially hearing impairment, has been found to be a potential risk factor in the elderly [20, 21].
- (b) Social isolation is another risk factor for the development of psychosis in the elderly [20, 21]. However, it has been suggested to be a phase that just precedes the onset of psychosis and may not be a risk factor [22].
- (c) As there is a preponderance of females in LOS, so this gender factor has also been postulated as a putative risk factor for the development of psychosis in the elderly

[23]. However, this has been refuted in a review [24].

- (d) Presence of cognitive deficits has also been suggested to be a risk factor [21, 24].
- (e) Other risk factors that have been suggested are history of psychotic symptoms [24], poor health [24], and use of polypharmacy [21].

Age of Onset and Its Relation to Outcome in Schizophrenia

The relationship between age of onset and outcome has been lucidly portrayed in a very recent review [25]. This review highlights the following:

- (a) Age of onset does not have any effect on remission; if at all there is any effect, it is very modest.
- (b) Similar was the situation with relapse, though there were studies which highlighted that onset of illness above the age of 25 years increased the chances of relapses.
- (c) Earlier age of onset resulted in more hospitalization. Those above 60 years had decreased risk of rehospitalization when compared to those who had their first admission before the age of 20 years. In addition, lower age was associated with a more negative outcome.
- (d) Overall, there was no statistically significant relationship between age of onset and employment status, but lower age at onset predicted poorer socio-occupational functioning, though two studies reported the opposite as well.
- (e) Overall lower age of onset was associated with poor global outcome.

Outcomes of EOS

Outcome of EOS is likely to be the same as that of schizophrenia in general. Overall, the remission rate varied from as low as 3% to as high as 64% [7]. This was mainly due to the way the sample was selected and even how remission itself was defined.

More interesting information regarding the course was garnered from those cases with schizophrenia which were followed up on a longitudinal basis. While 20% of patients were able to achieve remission, 20% worsened over time, while the course of the remaining 60% remained unchanged [11, 26]. There was initial fluctuation in the course of illness, usually in the first 5–10 years followed by a somewhat stable period or even improvement in symptoms as the individual with schizophrenia aged [11]. Though it appeared that older persons with schizophrenia remained asymptomatic and positive symptoms decreased over time, one thing that needed to be looked into is that there could be an increase in negative symptoms and cognitive decline which resulted in a picture of a calm and improved patient from the caregivers' perspective. This may be likely, as researchers have found out an age-related increase in negative symptoms and cognitive decline, as well as a positive correlation between these two domains [8]. Also a possibility exists that the older patients may not be reporting their positive symptoms [8]. Though there is cognitive impairment in individuals with schizophrenia, as reported in some studies, overall cognitive performance remains stable in older persons with schizophrenia [8, 11]. However, it has also been reported that there is cognitive decline in about a third of institutionalized patients [11].

Thus, there may be different outcomes related to cognitive deterioration. Outcome in EOS could vary considerably, including recovery, in a substantial proportion of individuals, depending upon the dwellings of the individuals, i.e., institution versus community [8].

Functional Outcome

When it comes to recovery itself, depending on whether the patients with EOS lived in a community or institutional setting, a review mentioned that significant improvement was noted in the range of 46–84% for clinical recovery and 21–77% for social recovery [8]. However, the same review mentions that recent short-term follow-up studies suggested that many elderly

patients with EOS had substantial level of impairment [8]. A review of the same has also suggested that EOS need not necessarily have a poor cognitive and functional outcome [27].

Outcomes of LOS

As highlighted earlier, due to various reasons, it is very difficult to follow up patients with LOS. There is a dearth of literature in this regard, and this makes it very challenging to track the outcome in LOS.

In terms of symptomatology, over the course of time, positive symptoms diminish, and there are hardly any new symptoms. There may be an increase in negative symptoms or the negative symptoms itself may reduce over time [27].

Though cognitive impairment is supposed to be a possible risk factor for development of LOS, a study in a community setting which compared individuals of EOS, LOS, and Alzheimer's disease (AD), regarding the change in cognitive functioning (changes at 1 and 2 years), found that EOS, LOS, and normal subjects had a relatively stable cognitive functioning, whereas those with AD had greater decline. Thus, there was no deterioration in the cognitive functioning in those with LOS [28]. However, some previous studies have reported an increase in, as well as intermediate rates of, deterioration in cognition as well [29].

An insight into the outcome of LOS has been provided by a 5-year follow-up study of Brodaty et al. [29] which found that overall patients had a worse outcome after 5 years in comparison to controls on several parameters like instrumental ADL and ADL scores, cognitive decline assessed with CDR, and cognitive decline scale, as well as decline in the score on MMSE (by 6.5 points over 5 years). Though three individuals out of ten (who were alive) in this study at the end of the 5-year period could not be interviewed, all seven individuals interviewed had symptoms of psychosis, and one even fulfilled the criterion A of DSM-IV for schizophrenia. This study also found that out of 19 cases that were assessed (including nine who had died and information as gathered from the informant), almost 50% had dementia

(five had met DSM-IV criteria for dementia). These perspectives thus bring into focus the existence of dementia in those with LOS, and clinicians need to be aware of this as it can be easily overlooked. However, the individuals with LOS and controls in this study did have significant differences in the presence of neurological abnormalities at the end of the 5-year period [29].

Functional Outcome in LOS

The social decline in those suffering with LOS may be less than that of those with EOS, as those with LOS may have already attained some developmental maturity [30], and this could be also the reason why better socio-occupational functioning is usually expected in those with LOS [20]. In fact, the 5-year outcome study mentioned previously commented that despite decline in several areas, global functioning (as assessed by GAF score) did not decline much in the LOS group, though it was somewhat lower than those of the controls [29].

Conclusions

Late-life schizophrenia is not entirely a homogeneous entity, comprised of EOS and LOS. The similarities between these types tend to outweigh the differences. Numerous risk factors have been identified related to the outcome. Structural and functional outcome tends to be better for EOS than for LOS. Nevertheless, these are tentative statements, as the amount of longitudinal evidence and literature available in this particular aspect of late-life schizophrenia is not robust enough to draw definitive conclusions.

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