Original Article

DOI: 10.7860/JCDR/2022/57582.17318

Psychiatry/Mental Health Section

Response of Antipsychotic Drugs in Late-onset and Early-onset Schizophrenia in the Vindhya Region, Central India: A Prospective Cohort Study

SUNEEL SINGH KUSHWAH[1], PRASHANT MARAVI[2], AKSHAT VARMA[3], DAISY RURE[4]

ABSTRACT

Introduction: Previous studies were predominantly on early-onset schizophrenia with little emphasis on clinical profile, therapeutic responsiveness and various investigational, biochemical and neuroimaging variables in Late-onset Schizophrenia (LOS), which is an emerging concern in elderly morbidity, and differs significantly from Early-onset Schizophrenia (EOS).

Aim: To study the clinical profile, and response to various antipsychotic drugs in LOS and compare it with EOS.

Materials and Methods: A clinical prospective cohort study was conducted in Shyam Shah Medical College, Rewa Madhya Pradesh, India, from January 2020 to June 2021, with baseline and follow-up assessment of psychotic and cognitive symptoms after four weeks using PANSS (Positive and Negative Syndrome Scale), MoCA (Montreal Cognitive Assessment) and BPRS (Brief Psychiatric Rating Scale) scales. A total of 51 patients were included in the study, divided into two groups of early and late onset, attending the out-patient and in-patient services during the period at the center and concomitant treatment with antipsychotics for four weeks. Statistical analysis was done in Statistical Package for Social Sciences (SPSS) version 21.0 with p-value of 0.05.

Results: A total of 51 patients, 27 in EOS group and 24 in LOS were included and analysed in the present study. The demographic profile of late and EOS varied in mean age with EOS at 30.11 years and LOS at 57.66 years), gender distribution predominantly males (n=19) in EOS and predominantly females (n=20) in LOS) and the average age of onset of EOS was 22.05 years and LOS was 55.54 years. The duration of illness in EOS 7.98 years and LOS was 2.12 years. The mean Positive and Negative Syndrome Scale score at baseline for EOS was 1.92±1.07 and LOS was 2.83±0.56 and four weeks for EOS was 1.70±0.91 and LOS was 2.83±0.56. The response in Positive and Negative Syndrome Scale at 4 weeks as well as individual domain scale score such as hallucinations, suspiciousness, blunted effect, emotional withdrawal, active social avoidance showed significant results in both EOS and LOS.

Conclusion: Schizophrenia can manifest for the first time in late life and manifestations of stringently defined schizophrenia is by no means confined to onset at younger ages. Although there are undoubted similarities between the symptoms of EOS and LOS, there are also clear differences, especially demographic and clinical characteristics, early identification of which will help in adequate intervention and prevention of further morbidity in the elderly.

Keywords: Clinical profile, Cognition, Rating scales, Response

INTRODUCTION

Schizophrenia though considered a disease of late adolescence and early adulthood [1] lately, the emergence of late-onset schizophrenia has become a major clinical concern, especially amongst the elderly populations. Schizophrenia is a chronic and severe mental disorder affecting twenty million people worldwide [2]. A review of studies on late-onset schizophrenia found that around twenty-three percent of patients with schizophrenia were accounted to have encountered the onset of the illness after age forty, with thirteen percent in the fifth decade of life, seven percent in the sixth decade, and three percent in later decades [3,4]. Among people aged 45 to 64 years, there is an incident rates of twelve point six (12.6) per 100,000 every year for new-onset schizophrenia. [4]. Schizophrenics are two to three times more likely to die earlier than the general population, which is often due to preventable physical diseases, including cardiovascular disorders, metabolic disease, and infections [5].

Though Dopamine is a key neurochemical in the pathophysiology of schizophrenia, with advancing age possibility of other non-dopaminergic pathophysiological factors also comes into focus, thus giving distinct characteristics to late-onset schizophrenia [6]. Late-onset schizophrenia also poses a diagnostic dilemma due to the existence of various degenerative disorders and other functional psychiatric disorders in old age, owing to which there are no separate diagnostic guidelines for late-onset schizophrenia in either ICD-10 DCR (International Classification of Diseases Diagnostic Criteria for Research-10) or DSM-5 (Diagnostic and Statistical Manual of mental disorders-5) [7,8].

Despite these problems, a relatively consistent clinical picture has been reported. Schizophrenia is a blend of trademark positive symptoms (delusions, hallucinations, conceptual disorganizations, etc.) and negative symptoms (apathy, blunting of affect, poor interaction, etc.) related with cognitive impairment and marked social or occupational dysfunction. Patients with the late-onset form, be that as it may, would in general have more persecutory delusions with and without hallucinations, organized delusions, and abusive auditory hallucinations or hallucinations with a running commentary [9]. The course of late-onset schizophrenia is usually chronic but may be interrupted by partial remissions and exacerbations. Patients may be quite responsive to antipsychotics used in lower doses like Risperidone (0.5 mg to 2 mg) Haloperidol (up to 5mg), Olanzapine (up to 5 mg), etc [10, 11]. Elderly patients are more susceptible to certain antipsychotic side effects, such as sedation, anticholinergic toxicity, and extrapyramidal symptoms. Atypical antipsychotics have become the agents of choice for older adults with psychosis, owing to their improved side-effect profile compared to conventional agents [12]. In terms of DALYs (Disability

Adjusted Life Years), schizophrenia ranked eighth, accounting for two-point six (2.6) percent of the total, and in terms of Years Lost to Disability (YLD), it was third, accounting to four-point nine (4.9) percent of the total [13,14].

It is therefore imperative to study the clinical profile, therapeutic responsiveness, and various investigational, biochemical, and neuroimaging variables in LOS in light of well-recognized EOS. Also, there is a dearth of data comparing EOS and LOS in Vindhya region which encompasses a large number of schizophrenia patients. Thus, the objective is (i) to study the clinical profile of LOS and EOS and (ii) the comparison of response to various antipsychotic drugs in LOS and EOS. The authors hypothesize that there will be a significant difference between both groups in terms of clinical profile and response.

MATERIALS AND METHODS

The present study was a clinical prospective cohort study from January 2020 to June 2021, took place at the Department of Psychiatry of Shyam Shah Medical College and Sanjay Gandhi Medical Hospital, Rewa, Madhya Pradesh, India, comprising of outpatient as well as inpatient subjects. The study was commenced after the approval from the department's scientific committee and Institutional Ethical and Scientific Committee (letter no. 9470/SS/PG/MC/2019).

Inclusion criteria: Patients of either sex, aged sixteen years and above, giving, informed consent, and fulfilling the criteria of schizophrenia disorder according to ICD-10 DCR [7] were included in the study.

Exclusion criteria: Patients with overt organic brain syndromes, space-occupying lesions, serious medical illness needing hospitalizations, co-morbid substance intake in dependence pattern and needing acute emergency treatment for physical/psychotic disorder were excluded from the study.

Considering the previous admission of LOS (two-three patients per month) thirty patients of late-onset and thirty patients of EOS were selected by purposive sampling according to the inclusion and exclusion criteria mentioned above. LOS has been defined as the onset of schizophrenia after 45 years, whereas, EOS as the onset before 18 years [15,16].

Procedure

After explanation of the rationale of the study and getting proper consent from patients and legally authorized representatives (such as family members), a thorough history, general, systemic and mental status examination was done to confirm the diagnosis and to record various socio-demographic clinical variables like age, gender, religion, marital status, socio-economic status, using Modified Kuppuswamy socioeconomic scale, 2019 etc [17]. Baseline investigations of complete blood haemogram, liver function, renal function, lipid profile, glucose level, serum electrolytes and electrocardiogram were done. Severity of psychosis and cognition was assessed on various rating scales (Brief Psychiatric Rating Scale (BPRS), Positive and Negative Syndrome Scale(PANSS), Montreal Cognitive Assessment (MoCA), scored on baseline, and at 4 weeks as most antipsychotics show response by this time [18,19].

Modified Brief Psychiatric Rating Scale (M-BPRS, John E. Overall and Donald R. Gorham, 1962): is a 18 item scale, scoring range from 1 (not present) to 7 (extremely severe);

Positive And Negative Syndrome Scale (PANSS, Stanley Kay, Lewis Opler and Abraham Fiszbein, 1987): is a 30-item scale (7 items each for positive and negative symptoms and 16 items for general psychopathological symptoms) scoring range from 1 (absent) to 7 (extreme);

Montreal Cognitive Assessment (MoCA, Ziad Nasreddine, 1966): is a screening instrument for cognitive impairment assessing visuospatial, naming, memory, attention, language, abstraction and orientation, with a total score of 30 (cut-off <26) [20-22]. All the scales were free. Therapeutic regime- the drug and doses- was also analysed as per the advice of consultants (MD Psychiatry) using PANSS and M-BPRS. Patients were prescribed Haloperidol (one EOS patient, 10 mg), Trifluoperazine (one EOS, 4 LOS, 5-10 mg), Olanzapine (2 EOS, 4 LOS, 10-20 mg), Risperidone (22 EOS, 16 LOS, 4-8 mg) and Clozapine (1 EOS, 200 mg).

STATISTICAL ANALYSIS

Statistical analysis was done using International Business Management (IBM) Statistical Package for Social Sciences (SPSS) statistics for windows version 21. 0 (IBM corp. Armonk, NY). The parametric data were presented in mean, standard deviation, percentages, and p-values. Continuous variables were compared using student's t-test, while discrete variables were compared using Chi-square test and non-parametric tests (Mann Whitney U test). The entire statistical test was two-sided, and level for statistical significance was 0.05.

RESULTS

A total of 100 patients suffering from schizophrenia were thoroughly screened. Out of these, 60 schizophrenic patients were selected by purposive sampling method, 30 patients in each early onset and late onset schizophrenia group who fulfilled inclusion criteria. Further nine patients, three in EOS group and six in late onset schizophrenia group could not complete this study due to severity of physical/psychiatric disorder needing emergency treatment referred to higher centre. Remaining 21 patients, 27 from EOS group and 24 from late onset schizophrenia group formed the sample of study and their baseline assessment was done following which another assessment was done after four weeks.

The demographic characteristics and psychiatric co-morbidity status of the two groups are shown in [Table/Fig-1]. As expected, mean age (EOS 30.11±6.96 years and LOS 57.66±10.14 years), mean age of onset (EOS 22.05±5.8 years and LOS 55.54±10.23 years) and mean duration of illness (EOS 7.98±5.19 and LOS 2.12±1.93 years) of both the groups was significantly varied. Also subjects of EOS were educated upto middle school (11 (40.8%) whereas that of LOS were illiterate (n=14, 58.3). Subjects of both groups were mostly married (n=14 (51.9%) for EOS and n=16 (66.7%) for LOS), belonging to upper lower socioeconomic class (n=14 (51.8%) EOS, n=16 (66.7%) LOS), residing in rural locality (n=19 (70.4%) EOS and n=20 (91.7%) LOS) and unemployed (n=19 (70.4%) EOS, n=20 (83.4%) LOS). Family history of psychiatric illness was uncommon in both groups, whereas n=6 (22.22%) for EOS and n=6 (25%) for LOS, precipitating factors were noted as n=2 (7.40%) in EOS and n=2 (29.16%) in LOS, 8% of patients had another co-morbid psychiatric condition in EOS as well as LOS.

Baseline and four weeks assessment of PANSS and MoCA is given in [Table/Fig-2]. PANSS composite scale score at baseline and 4 weeks were significantly different for EOS and LOS, however there was no change in score for LOS at 4 weeks. PANSS positive scale score and PANSS general psychopathology scale score of EOS and LOS was significantly different at baseline and 4 weeks, however, PANSS negative scale score for EOS and LOS was not different significantly at baseline.

PANSS individual domain score [Table/Fig-3] at baseline and 4 weeks within EOS changed significantly in conceptual disorganisation, hallucination, suspiciousness, grandiosity, blunted affect, emotional withdrawal, rapport, passive apathetic social withdrawal, difficulty in abstract thinking, lack of spontaneity and flow of conversation, mannerisms, motor retardation, unusual thought content, lack of judgement and insight, disturbance of volition, pre-occupation and active social avoidance. Whereas PANSS individual domain score at baseline and 4 weeks in late onset schizophrenia changed significantly in delusion, hallucination, suspiciousness, blunted affect,

Variables	Early Onset Schizophrenia (n=27)	Late Onset Schizophrenia (n=24)	p-value
Age (years)	30.11±6.96	57.66±10.14	**<0.001**
Gender	70.3% males (n=19)	83.3% females (n=20)	**<0.001**
Married	51.9% (n=14)	66.7% (n=16)	**<0.001**
SES	Upper lower (n=14, 51.8%)	Upper lower (n=16, 66.7%) Lower middle (n=8, 33.3%)	0.79
	Lower middle (n= 5,18.5%)		
	Upper middle (n=4, 14.9%)		
	Upper (n=3,11%)		
	Lower (n=1, 3.7%)		
Education	Middle (n=11, 40.8%)	Illiterate (n=14, 58.4%)	**<0.001**
Occupation	Unemployed (n=19, 70.4%)	Unemployed (n=20, 83.4%)	0.286
Residence	Rural (n=19, 70.4%)	Rural (n=22, 91.7%)	0.056
Family type	Nuclear (n=23, 85.1%)	Nuclear (n=22, 91.6%)	0.453
Age of onset, (mean±SD, years)	22.05±5.8	55.54±10.23	**<0.001**
Duration of illness, (mean±SD, years)	7.98±5.19	2.12±1.93	**<0.001**
Course of illness	Continuous (n=20, 74%)	Continuous (n=24, 100%)	0.065
Presence of precipitating factor	22.2% (n=6)	25% (n=6)	0.815
Positive family history of psychiatric illness	11.1% (n=3)	8.3%(n=2)	0.362
Presence of psychiatric co-morbidity	7.4% (n=2)	8.3% (n=2)	0.258

[Table/Fig-1]: General demographic characteristics.
SES= Socio-economic status, p-value <0.05 is statistically significant (Student t-test applied for continuous data and Mann-Whitney U test for nominal and ordinal data); Bold p-values are significant

Variables	Early onset Schizophrenia (n=27)	Late onset Schizophrenia (n=24)	p-value
PANSS mean composite scale score, baseline	1.92±1.07	2.83±0.56	**<0.001**
PANSS mean composite scale score, 4 weeks	1.70±0.91	2.83±0.56	**<0.001**
PANSS mean positive scale score, baseline	19.77±5.91	20.50±4.30	**0.032**
PANSS mean positive scale score, 4 weeks	10.77± 2.27	11.66± 1.78	**0.033**
PANSS mean negative scale score, baseline	21.03± 8.37	14.25± 7.43	0.132
PANSS mean negative scale score, 4 weeks	12.74 ±4.46	9.16 ±2.31	**0.011**
PANSS mean general psychopathology scale score, baseline	35.00± 4.49	30.08± 5.88	**0.025**
PANSS mean general psychopathology scale score, 4 weeks	22.07± 2.05	19.83 ±2.63	**0.010**
MoCA mean score, baseline	13.25± 5.87	12.08± 4.5	0.344
MoCA mean score, 4 weeks	22.44 ±3.16	20.08 ±2.96	0.336
BPRS scale mean score, baseline	36.59±4.05	33.33±4.41	0.484
BPRS scale mean score, 4 weeks	23.11±2.67	22.33±1.52	0.145

[Table/Fig-2]: Scores of PANSS, MoCA and BPRS scale in Early onset and Late onset Schizophrenia.
PANSS= Positive and Negative Syndrome Scale, BPRS= Brief Psychiatric Rating Scale, MoCA= Montreal Cognitive Assessment, p-value <0.05 is statistically significant (Student t-test applied)

	Early Onset Schizophrenia (n=27)			Late Onset Schizophrenia (n=24)		
Domain	At baseline	At 4 weeks	p-value	At baseline	At 4 weeks	p-value
Delusions	3.88±2.62	2.03±1.12	0.837	5.00±0.88	2.50±0.97	**0.007**
Conceptual disorganisation	2.66±1.70	1.51±0.84	**<0.001**	1.16±1.55	1.0±0.00	0.6155
Hallucinations	4.81±1.49	2.29±0.95	**<0.001**	4.88±0.97	2.33±0.76	**<0.001**
Suspiciousness	3.03±0.72	1.77±0.00	**<0.001**	4.91±1.83	2.83±0.00	**<0.001**
Excitement	1.00±1.56	1.00±0.192	1.0000	1.66±1.10	1.00±0.00	**0.0051**
Grandiosity	1.92±2.62	1.03±1.18	**<0.001**	1.00±1.41	1.00±1.16	1.0000
Hostility	2.4±1.3	1.11±0.42	0.302	1.91±1.04	1±0.00	**0.0001**
Blunted affect	3.03±1.72	1.74±0.90	**<0.001**	1.41±1.96	1.08±0.28	**<0.001**
Emotional withdrawal	4.22±1.86	2.37±1.11	**<0.001**	2.166±1.21	1.25±0.607	**<0.001**
Poor rapport	1.55±1.12	1.55±0.38	**0.005**	1.41±1.14	1.0±0.00	0.0847
Passive apathetic social withdrawal	4.22±2.32	4.22±2.62	**0.014**	2.08±0.88	1.25±0.607	**<0.001**
Difficulty in abstract thinking	4.37±1.57	2.74±1.7	**0.043**	4.00±0.00	2.41±0.77	**<0.001**
Lack of spontaneity and flow of conversation	2.22±1.76	1.33±1.49	**0.002**	1.50±0.76	1.08±0.28	**<0.001**
Stereotyped thinking	1.40±0.79	1.0±0.72	0.0573	1.66±0.60	1.08±0.28	**<0.001**
Somatic concern	1.29±0.77	1.00±1.56	0.3904	2.25±0.56	1.5±0.88	**<0.001**

Anxiety	1.00±0.00	1.00±2.62	0.3904	1.91±0.86	1.16±0.38	**<0.001**
Guilt	1.07±0.38	1.00±1.30	0.7893	1.00±1.69	1.00±0.00	1.0000
Tension	1.07±0.38	1.00±0.192	0.842	1.5±1.38	1.16±0.58	0.2716
Mannerism	1.77±1.69	1.55±1.94	**<0.001**	1.5±0.77	1.00±0.00	**0.0026**
Depression	1.00±0.00	1.00±0.00	-	1.58±1.79	1.00±0.00	0.1193
Motor retardation	1.48±0.00	1.03±0.192	**<0.001**	1.0±1.67	1.00±0.00	1.0000
Uncooperativeness	1.55±1.25	1.00±0.00	**0.0263**	1.33±1.32	1.00±0.00	0.2269
Unusual thought content	2.11±1.12	1.03±0.192	**<0.001**	1.25±0.60	1.00±0.00	**0.0470**
Disorientation	1.07±1.36	1.37±0.192	0.842	1.16±0.56	1.00±0.00	0.1683
Poor attention	1.44±0.38	1.00±0.00	**0.0001**	1.33±0.86	1.08±0.28	0.1823
Lack of judgement and insight	6.33±0.89	3.96±0.85	**0.028**	4.91±1.69	2.66±1.12	**0.001**
Disturbance of volition	3.03±0.83	1.55±0.80	**0.001**	4.91±1.38	1.33±0.63	**<0.001**
Impulse control	2.07±1.87	1.00±0.00	**0.0045**	1.41±0.77	1.00±0.00	**0.0122**
Preoccupation	5.81±1.38	2.74±0.71	**0.001**	3.5±1.79	1.66±0.86	**<0.001**
Active social avoidance	2.85±0.92	1.55±1.05	**<0.001**	2.25±1.67	1.25±0.63	**<0.001**

[Table/Fig-3]: PANSS individual domain scale score.
(-) No statistics computed because PANSS at 4 weeks is constant; p-value <0.05 is statistically significant; Bold p-values are significant

emotional withdrawal, passive apathetic social withdrawal, difficulty in abstract thinking, lack of spontaneity and flow of conversation, stereotype, somatic concern, anxiety, lack of judgement and insight, disturbance in volition, pre-occupation and active social avoidance.

[Table/Fig-4-6] show response in PANSS scale parameters, antipsychotics prescribed and gender relationship with response. Response at 4 weeks is defined as 50% reduction in baseline PANSS scale score. Significantly more response was noted in EOS PANSS [Table/Fig-5], response was seen in 10 patients in EOS group (one patient with haloperidol, nine patients with risperidone) and 2 patients in LOS group (with risperidone). Furthermore, out of 28 females and 23 males, 6 females and males showed response [Table/Fig-6].

DISCUSSION

Earlier authors regarded early and late-onset forms of schizophrenia as the same disorder, concentrating on the similarities and ignoring the differences between them. Although, there are undoubted similarities between the symptoms of early and late-onset schizophrenia, there are also clear differences. Late-onset schizophrenia is similar, but not identical to the early-onset illness, at least in its phenotypic expression. Socio-economic variables like mean age (30.11±6.96 years for early onset and 57.66±10.14 years for late onset); gender distribution (70.3% males in EOS and 83.3% females in LOS); socioeconomic distribution (upper lower); marital status; education; and residence (majority rural in both groups) were similar to Jeste DV et al., Roth M, Van Os et al., Sham PC et al., Lehman SW, Girard C and Simard M, Croudace TJ et al., clinical profile variables as age of onset (22.05±5.8 years for EOS; 55.54±10.23 years for LOS), duration of illness (7.98±5.19 years for EOS; 2.12±1.93 years for LOS), psychiatric (7.4% in EOS; 8.3% in LOS) co- morbidity, family history of psychiatric illness (11.1% in EOS and 8.3% in LOS) and precipitating factors (22.2% in EOS and

Variables	Early onset schizophrenia (n=27)	Late onset schizophrenia (n=24)	p-value
Response in PANSS Positive scale	10 (37.03%)	2 (8.33%)	**0.016**
Response in PANSS Negative scale	0	0	No response
Response in PANSS General Psychopathology scale	0	0	No response

[Table/Fig-4]: Response in PANSS Scale.
p-value <0.05 is statistically significant (Student t-test) PANSS= Positive and Negative Syndrome Scale

Group			Haloperidol	Trifluperazine	Olanzapine	Risperidone	Clozapine	Total
Early onset schizophrenia	Response	Yes	1	0	0	9	0	10
		No	0	1	2	13	1	17
		Total	1	1	2	22	1	27
Late onset schizophrenia	Response	Yes	0	0	0	2	0	2
		No	0	4	4	14	0	22
		Total	0	4	4	16	0	24

[Table/Fig-5]: Response in Positive PANSS scale score and Antipsychotics.
PANSS: Positive and Negative Syndrome Scale

Gender		Response	No response
Male	Count	6	17
	% within sex	26.1	73.9
	% within response	50.0	43.6
Female	Count	6	22
	% within sex	21.4	78.6
	% within response	50.0	56.4
Total	Count	12	39
	% within total response	23.5	76.5

[Table/Fig-6]: Gender and PANSS positive scale score response.
Chi-square value is 0.696 which is not significant as p-value >0.05

positive scale as compared to LOS [Table/Fig-4], whereas, no response was seen for PANSS negative and general psychopathology scale. In

25% in LOS) corresponds with previous studies [23-29]. As would be expected, age of patients, age of onset of illness and duration of illness were significantly different in both groups, however, in addition to the gender, marital status and education were also distinct in both schizophrenia groups, which may be attributable to the region itself and the age of onset of illness. In PANSS scale, delusions and hallucinations are the common symptoms and negative symptoms are less common, in accordance with other published reports by C. Huang and Zhang Y-L and X. Huang et al. [30, 31]. The mean positive scale score of 19.77 was comparable with previous studies Girard C and Simard M [28]. Late age of onset has been associated with paranoid-hallucinatory symptoms and paranoid schizophrenia in subtypes had reported that negative symptoms and thought disorder occurred to a significantly lesser degree in the LOS group. The relatively same MoCA score at baseline and 4 weeks in both groups point towards the stability of cognitive impairment over time [32,33]. Both LOS (22 out of 24, 91.7%) and EOS (22 out of 27, 81.5%) patients had moderate to severe cognitive impairment in MoCA scale which coincides with available data, which may be due to sensitivity of MoCA scale and the severity of patients reaching tertiary centres [34]. The slightly higher cognitive impairment in LOS group may be due to slightly higher illiteracy in this group.

In EOS group, response (PANSS positive scale score at 4 weeks ≤50% of PANSS positive scale score at baseline) was seen in 10 out of 27, 37% of patients, meanwhile it was seen in 2 out of 24, 8.33% of patients of LOS group There was no response in PANSS negative scale and general psychopathology scale after 4 weeks follow up in both groups. Response was seen with Risperidone in nine patients of EOS group and two patients of LOS group. In EOS group, no response was seen with Trifluoperazine, olanzapine, clozapine, whereas in LOS group, no response was seen with Trifluoperazine and olanzapine, which is on par with our initial hypothesis. Risperidone was the highest prescribed antipsychotic in both EOS and LOS group. The confounding factor here could be due to inappropriate and in equivalent dosing, poor drug compliance and risperidone was the highest prescribed antipsychotic. A Cochrane Review conducted in 2012 regarding the use of antipsychotics in LOS found that symptoms decreased in both treatment arms on the Brief Psychiatric Rating Scale [31, 35]. In short, there was not enough trial-based evidence upon which to base guidelines for use of antipsychotics in LOS. Jeste DV et al., (2003) concluded that stable elderly patients with chronic schizophrenia receiving appropriate doses of risperidone or olanzapine over eight-week period experienced significant reductions in the severity of psychotic and extrapyramidal symptoms, with a relatively low risk of side effects [36]. In comparison to the present study, only risperidone showed significant improvement. This may be due to Risperidone is the highest prescribed antipsychotic in both early and late onset schizophrenia group in the present study. A short-term outcome study of broad psychotic disorders would be necessary to describe potential similarities and differences in psychopathology between early and late-onset schizophrenia more precisely. Information regarding elderly LOS is limited, and further large scale longitudinal studies encompassing other community subsets are required.Further longitudinal studies are needed for improving understanding of the cause- effect relationship. The assessment did not include imaging or biological factors; these factors should be included in future studies for analysis. Further research into the epidemiology and phenomenology of such patients should seek to integrate findings with other factors pertaining to the etiology of late-onset schizophrenia. Further systematic research into its epidemiology, phenomenology, and genetics, other biological and psychosocial issues, and course and outcome are necessary for a better understanding of this condition.

Limitation(s)

Major limitation of this study is the sample size, which was not large and constituted only of institutionalized patients, thus hindering the generalizability. Also there was no blinding in this study as compared to other studies. Since subjects with diagnosis on last day of index hospitalization were included, there is a possibility that some psychotic patients who may receive diagnosis of schizophrenia in future were left out.

CONCLUSION(S)

It was concluded that schizophrenia can manifest for the first time in late life and manifestations of stringently defined schizophrenia is by no means confined to onset at younger ages. Delusions and hallucinations are the common symptoms and negative symptoms are less common, in accordance with other published reports. This study has also revealed the other most consistent finding that women were more prevalent than men in late-onset schizophrenia. The authors in the present study found that both LOS and EOS patients had cognitive and functioning impairment with poor global outcomes. An association of LOS with lower educational levels was observed in this study. There is only response in positive symptoms after 4 weeks of prescribed antipsychotic treatment in both EOS and LOS group, significantly more in EOS. Late-onset schizophrenia is largely ignored and understudied as evidenced by scarcity of literature on the subject. One reason for this is a widespread failure to recognize it as a condition apart from EOS which, as such, deserves an investigative attention. The current study has shown that it is possible on clinical grounds to recognize separate early and late onset schizophrenia syndromes.

REFERENCES

[1] Häfner H, Maurer K, Löffler W, Fätkenheuer B, an der Heiden W, Riecher-Rössler A, et al. The epidemiology of early schizophrenia. Influence of age and gender on onset and early course. Br J Psychiatry Suppl. 1994; 23:29-38. PMID: 8037899.

[2] James SL, Abate D, Abate KH, Abay SM, Abbafati C, Abbasi N, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: A systematic analysis for the Global Burden of Disease Study 2017. The Lancet. 2018;392(10159):1789-58.

[3] Harris MJ, Jeste DV. Late-onset Schizophrenia: An Overview. Schizophr Bull. 1988;14(1):39-55.

[4] Castle DJ, Murray RM. The Epidemiology of Late-onset Schizophrenia. Schizophr Bull. 1993;19(4):691-700.

[5] Laursen TM, Nordentoft M, Mortensen PB. Excess early mortality in schizophrenia. Annu Rev Clin Psychol. 2014;10:425-48. Doi: 10.1146/annurev-clinpsy-032813-153657. Epub 2013 Dec 2.

[6] McCutcheon RA, Krystal JH, Howes OD. Dopamine and glutamate in schizophrenia: biology, symptoms and treatment. World Psychiatry. 2020;19(1):15-33.

[7] WHO. International classification of diseases-10 Diagnostic criteria for research of mental and behavioural illness [Internet]. [cited 2021 Oct 29]. Available from: https://www.who.int/classifications/icd/en/GRNBOOK.pdf.

[8] DSM-5 [Internet]. [cited 2021 Nov 1]. Available from: https://www.psychiatry.org/psychiatrists/practice/dsm.

[9] Howard R, Castle D, Wessely S, Murray R. A comparative study of 470 cases of early-onset and late-onset schizophrenia. Br J Psychiatry. 1993;163:352-57. Doi: 10.1192/bjp.163.3.352.

[10] Howard R, Rabins PV, Seeman MV, Jeste DV. Late-onset schizophrenia and very-late-onset schizophrenia-like psychosis: An international consensus. The International Late-Onset Schizophrenia Group. Am J Psychiatry. 2000;157(2):172-78.

[11] Vahia IV, Palmer BW, Depp C, Fellows I, Golshan S, Kraemer HC, et al. Is Late-Onset Schizophrenia a Subtype of Schizophrenia? Acta Psychiatr Scand. 2010;122(5):414-26.

[12] Gareri P, Segura-García C, Manfredi VGL, Bruni A, Ciambrone P, Cerminara G, et al. Use of atypical antipsychotics in the elderly: A clinical review. Clin Interv Aging. 2014;9:1363-73. Doi: 10.2147/CIA.S63942. eCollection 2014.

[13] Benjamin James Saddock, Saddock VA, Ruiz P. Comprehensive textbook of Psychiatry. 10th ed. Vol. 1.

[14] WHO | Global Burden of Disease (GBD) 2000 estimates [Internet]. WHO. World Health Organization; [cited 2020 Oct 21]. Available from: https://www. who.int/healthinfo/global_burden_disease/estimates_regional_2000/en/.

[15] Folsom DP, Lebowitz BD, Lindamer LA, Palmer BW, Patterson TL, Jeste DV. Schizophrenia in late life: Emerging issues. Dialogues Clin Neurosci. 2006;8(1):45-52.

[16] Driver DI, Gogtay N, Rapoport JL. Childhood Onset Schizophrenia and Early Onset Schizophrenia spectrum disorders. Child Adolesc Psychiatr Clin N Am. 2013;22(4):539-55.

[17] Mohd Saleem S. Modified Kuppuswamy socioeconomic scale updated for the year 2020. IJFCM. 2020;7(1):1-3.

[18] Bunney BS. Dopaminergic blocking effects of antipsychotic drugs. J Psychiatr Res. 1974;11:72-73. Available on: https://doi.org/10.1016/0022-3956(74)90074-0. PMid: 4156793.
[19] Bunney BS, Walters JR, Roth RH, Aghajanian GK. Dopaminergic neurons: effect of antipsychotic drugs and amphetamine on single cell activity. J Pharmacol Exp Ther 1973;185(3):560-71.
[20] BPRS Brief Psychiatric Rating Scale [Internet]. Psychiatric Times. [cited 2022 Jun 30]. Available from: https://www.psychiatrictimes.com/view/bprs-brief-psychiatric-rating-scale.
[21] Positive and Negative Syndrome Scale. In: Wikipedia [Internet]. 2022 [cited 2022 Jun 30]. Available from: https://en.wikipedia.org/w/index.php?title=Positive_and_Negative_Syndrome_Scale&oldid=1079896630.
[22] Montreal Cognitive Assessment. In: Wikipedia [Internet]. 2022 [cited 2022 Jun 30]. Available from: https://en.wikipedia.org/w/index.php?title=Montreal_Cognitive_Assessment&oldid=1079896338.
[23] Jeste DV, Symonds LL, Harris MJ, Paulsen JS, Palmer BW, Heaton RK. Nondementia nonpraecox dementia praecox? Lateonset schizophrenia. Am J Geriatr Psychiatry.1997;5(4):302-17.
[24] Roth M. The Natural History of Mental Disorder in Old Age. J Ment Sci. 1955;101(423):281-01.
[25] Van Os J, Howard R, Takei N, Murray R. Increasing age is a risk factor for psychosis in the elderly. Soc Psychiatry Psychiatr Epidemiol. 1995;30(4):161-64.
[26] Sham PC, Castle DJ, Wessely S, Farmer AE, Murray RM. Further exploration of a latent class typology of schizophrenia. Schizophr Res. 1996;20(1-2):105-15.
[27] Lehmann SW. Psychiatric disorders in older women. Int Rev Psychiatry. 2003;15(3):269-79.
[28] Girard C, Simard M. Clinical characterization of late- and very late-onset first psychotic episode in psychiatric inpatients. Am J Geriatr Psychiatry Off J Am Assoc Geriatr Psychiatry. 2008;16(6):478-87.
[29] Croudace TJ, Kayne R, Jones PB, Harrison GL. Non-linear relationship between an index of social deprivation, psychiatric admission prevalence and the incidence of psychosis. Psychol Med. 2000;30(1):177-85.
[30] Huang C, Zhang Y-L. Clinical differences between late-onset and early-onset chronically hospitalized elderly schizophrenic patients in Taiwan. Int J Geriatr Psychiatry. 2009;24(10):1166-72.
[31] Huang X, Zhong Z, Zhang J. The effects of risperidone and olanzapine on the glucose metabolism and lipid metabolism in elderly patients with schizophrenia. Journal of Clinical Psychosomatic Diseases. 2007;13(1):1-3.
[32] Harish MG, Suresh KP, Rajan I, Reddy YC, Khanna S. Phenomenological study of late-onset schizophrenia. Indian J Psychiatry. 1996;38(4):231-35.
[33] Palmer BW, Bondi MW, Twamley EW, Thal L, Golshan S, Jeste DV. Are late-onset schizophrenia spectrum disorders neurodegenerative conditions? Annual rates of change on two dementia measures. J Neuropsychiatry Clin Neurosci. 2003 Winter;15(1):45-52.
[34] Wu C, Dagg P, Molgat C. A pilot study to measure cognitive impairment in patients with severe schizophrenia with the Montreal Cognitive Assessment (MoCA). Schizophr Res. 2014;158(1–3):151-55.
[35] Essali A, Ali G. Antipsychotic drug treatment for elderly people with late-onset schizophrenia. Cochrane Database Syst Rev. 2012;2012(2):CD004162.
[36] Jeste DV, Barak Y, Madhusoodanan S, Grossman F, Gharabawi G. International multisite double-blind trial of the atypical antipsychotics risperidone and olanzapine in 175 elderly patients with chronic schizophrenia. Am J Geriatr Psychiatry Off J Am Assoc Geriatr Psychiatry. 2003;11(6):638-47.

PARTICULARS OF CONTRIBUTORS:
1. Senior Resident, Department of Psychiatry, Gandhi Medical College, Bhopal, Madhya Pradesh, India.
2. Senior Resident, Department of Psychiatry, Shyam Shah College, Rewa, Madhya Pradesh, India.
3. Senior Resident, Department of Psychiatry, Shyam Shah College, Rewa, Madhya Pradesh, India.
4. Senior Resident, Department of Psychiatry, Nandkumar Singh Chouhan Government Medical College, Khandwa, Madhya Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Daisy Rure,
Senior Resident, Department of Psychiatry, Nandkumar Singh Chouhan Government Medical College, Khandwa, Madhya Pradesh, India.
E-mail: daisy.rure@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: May 12, 2022
- Manual Googling: Nov 11, 2022
- iThenticate Software: Nov 21, 2022 (14%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **May 05, 2022**
Date of Peer Review: **Jun 23, 2022**
Date of Acceptance: **Nov 26, 2022**
Date of Publishing: **Dec 01, 2022**