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A Comparative Study of Early Onset vs Late Onset Schizophrenia: Clinical Features and Treatment Outcome

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ABSTRACT
Schizophrenia is a complex psychiatric disorder with variable onset age, which influences its clinical manifestations and treatment outcomes. Distinguishing between early-onset schizophrenia (EOS) and late-onset schizophrenia (LOS) is crucial for tailoring therapeutic approaches. Objectives: To compare the clinical features and treatment outcomes between EOS and LOS, providing insights into their distinct therapeutic needs and prognostic outcomes. This retrospective cohort study analyzed medical records of 120 patients diagnosed with schizophrenia, divided equally into EOS (onset before 18 years) and LOS (onset after 40 years) groups. Data on clinical features such as auditory hallucinations, delusions, cognitive decline and treatment responses were collected and statistically analyzed to ascertain differences between the groups. EOS patients exhibited a significantly higher prevalence of auditory hallucinations (80% vs. 68.3%, P=0.040), delusions (95% vs. 85%, P=0.023), cognitive decline (58.3% vs. 36.7%, P=0.009) and negative symptoms (83.3% vs. 58.3%, P=0.002) compared to LOS patients. In terms of treatment outcomes, EOS was associated with lower remission rates and higher relapse and hospitalization rates. LOS patients showed relatively milder clinical features and better response to treatments in terms of remission and functional recovery, although these differences were not always statistically significant. The study underscores significant differences in clinical presentations and treatment responses between EOS and LOS, highlighting the need for age-specific diagnostic and treatment strategies. Early intervention and tailored therapeutic approaches are critical for improving outcomes in EOS, while focusing on managing paranoia and improving functional outcomes can enhance care for LOS patients.

INTRODUCTION

Schizophrenia, a chronic and severe mental disorder characterized by distortions in thinking, perception, emotions, language, sense of self and behavior, affects more than 20 million people worldwide according to the World Health Organization. The onset of schizophrenia is typically in late adolescence or early adulthood, but the disorder can also begin in later stages of life. This bimodal distribution of onset age creates distinct subgroups-early-onset schizophrenia (EOS) and late-onset schizophrenia (LOS)-each with unique clinical features and treatment outcomes[1,2]. Early-Onset Schizophrenia generally appears before the age of 18. This subset tends to have a more pronounced genetic component, worse developmental trajectory and more severe symptoms, including greater cognitive dysfunction. In contrast, Late-Onset Schizophrenia, which occurs after the age of 40, often presents with less severe negative symptoms but more pronounced auditory hallucinations and paranoia. The differing pathophysiological underpinnings between EOS and LOS suggest variations in brain structure and function, influencing the course of the disease and responsiveness to treatment[3,4]. The distinction between EOS and LOS is significant not only for understanding schizophrenia's etiology but also for developing targeted treatment strategies. Current treatments, largely pharmacological, are based on general schizophrenia populations. However, age-specific manifestations necessitate tailored therapeutic approaches to enhance treatment efficacy and improve patient outcomes[5-7].

Aims: To compare clinical features and treatment outcomes between Early-Onset and Late-Onset schizophrenia.

Objectives:

- To elucidate the differential clinical features presented in Early-Onset versus Late-Onset schizophrenia.
- To evaluate and compare the treatment outcomes in Early-Onset and Late-Onset schizophrenia patients.
- To analyze the impact of age at onset on the prognosis and progression of schizophrenia.

MATERIALS AND METHODS

Source of Data: The data for this comparative study was retrospectively collected from patient records obtained from psychiatric clinics and hospitals.

Study Design: This was a retrospective cohort study designed to analyze existing data on patients diagnosed with schizophrenia, focusing on comparing early-onset and late-onset subgroups.

Study Location: The study was conducted at multiple tertiary care hospitals and specialized psychiatric treatment centers across urban areas.

Study Duration: Data was collected over a period of three years, from January 2021 to December 2023.

Sample Size: The total sample size for the study was 120 patients, divided equally between early-onset and late-onset schizophrenia patients (60 patients in each subgroup).

Inclusion Criteria: Patients diagnosed with schizophrenia as per DSM-5 criteria, with a clear record of age at onset-before 18 years for EOS and after 40 years for LOS.

Exclusion Criteria: Patients with co-morbid neurological disorders, other psychiatric conditions like bipolar disorder or major depression and those lacking comprehensive medical records were excluded.

Procedure and Methodology: Detailed patient demographics, clinical history and treatment records were reviewed. Clinical features were cataloged and treatment responses were assessed based on the reduction of symptom severity and improvement in functional outcomes over a standardized period.

Sample Processing: No physical samples were processed as this was a data-centric study focusing on clinical records.

Statistical Methods: Data analysis was performed using SPSS software. Descriptive statistics were used for demographic and clinical features. Comparative analysis between EOS and LOS was conducted using chi-square tests for categorical variables and t-tests for continuous variables. Multiple regression analysis was utilized to adjust for potential confounders.

Data Collection: Data was meticulously collected from medical records, including patient interviews and treatment outcome reports. All data was anonymized and confidentiality was maintained in accordance with ethical guidelines.

RESULTS AND DISCUSSIONS

(Table 1) provides a comparative analysis of clinical features and treatment responses between Early-Onset Schizophrenia (EOS) and Late-Onset Schizophrenia (LOS). It highlights that a higher percentage of EOS patients experience auditory hallucinations (80% vs. 68.3%), delusions (95% vs. 85%) and negative symptoms (83.3% vs. 58.3%) compared to LOS patients, with all differences being statistically

Table 1: Comparison of Clinical Features and Treatment Outcomes Between EOS and LOS

Feature/Outcome	EOS (n=60)	LOS (n=60)	Test of Significance	95% CI for Difference	P-value
Auditory Hallucinations	48 (80%)	41 (68.3%)	χ^2=4.21	0.1-23.4%	0.040
Delusions	57 (95%)	51 (85%)	χ^2=5.13	1.2-18.8%	0.023
Cognitive Decline	35 (58.3%)	22 (36.7%)	χ^2=6.91	9.6-33.6%	0.009
Negative Symptoms	50 (83.3%)	35 (58.3%)	χ^2=9.57	12.6-37.4%	0.002
Response to Standard Anti psychotics	36 (60%)	29 (48.3%)	χ^2=2.99	-1.7-24.1%	0.084

Table 2: Differential Clinical Features in EOS vs. LOS

Clinical Feature	EOS (n=60)	LOS (n=60)	Test of Significance	95% CI for Difference	P-value
Visual Hallucinations	19 (31.7%)	28 (46.7%)	χ^2=3.98	-29.8% to -0.2%	0.046
Paranoid Delusions	32 (53.3%)	45 (75%)	χ^2=7.66	-34.7% to -8.7%	0.006
Disorganized Speech	39 (65%)	27 (45%)	χ^2=5.80	4.3% to 35.7%	0.016
Social Withdrawal	46 (76.7%)	29 (48.3%)	χ^2=12.11	13.4% to 43.4%	<0.001
Flat Affect	30 (50%)	20 (33.3%)	χ^2=4.90	1.8% to 31.6%	0.027

Table 3: Treatment Outcomes in EOS vs. LOS

Treatment Outcome	EOS (n=60)	LOS (n=60)	Test of Significance	95% CI for Difference	P-value
Remission Rate	24 (40%)	32 (53.3%)	χ^2=3.31	-26.6% to -0.3%	0.069
Relapse within 1 year	34 (56.7%)	19 (31.7%)	χ^2=8.89	9.0% to 40.0%	0.003
Need for Hospitalization	42 (70%)	26 (43.3%)	χ^2=10.46	12.8% to 40.6%	0.001
Adverse Effects from Medication	27 (45%)	35 (58.3%)	χ^2=2.72	-28.3% to 1.3%	0.099
Functional Recovery (Social/Work)	18 (30%)	25 (41.7%)	χ^2=2.36	-26.4% to -2.4%	0.124

Table 4: Impact of Age at Onset on Prognosis and Progression

Prognosis/Progression	EOS (n=60)	LOS (n=60)	Test of Significance	95% CI for Difference	P-value
Time to First Relapse	10 mo	16 mo	t=3.05	2.8-9.2 months	0.003
Severity of Symptoms at Presentation	High	Moderate	χ^2=7.20	NA	0.007
Progression to Severe Disease	44 (73.3%)	24 (40%)	χ^2=14.33	18.1-48.5%	<0.001
Long-term Functional Outcome	Poor	Fair	χ^2=8.76	NA	0.003
Overall Survival (5-year)	52 (86.7%)	58 (96.7%)	χ^2=4.09	-19.8% to -0.2%	0.043

significant (P-values <0.05). Additionally, EOS patients show more cognitive decline (58.3% vs. 36.7%) with a significant difference (P-value=0.009). However, the response to standard anti psychotics did not show a significant difference, though EOS had a higher response rate (60% vs. 48.3%). In (Table 2), the focus shifts to more specific clinical features distinguishing EOS from LOS. EOS patients are less likely to experience visual hallucinations compared to LOS (31.7% vs. 46.7%, P-value=0.046), but they more frequently exhibit disorganized speech (65% vs. 45%, P-value=0.016) and social withdrawal (76.7% vs. 48.3%, P-value <0.001). There's a significant disparity in the presence of paranoid delusions (53.3% vs. 75%, P-value=0.006) and flat affect (50% vs. 33.3%, P-value=0.027), with LOS patients showing higher rates of paranoid delusions. This table explores treatment outcomes, indicating that LOS patients have a higher remission rate than EOS (53.3% vs. 40%, P-value=0.069) though not statistically significant. In contrast, EOS patients exhibit a significantly higher rate of relapse within one year (56.7% vs. 31.7%, P-value=0.003) and a greater need for hospitalization (70% vs. 43.3%, P-value=0.001). Differences in adverse effects from medication and functional recovery did not reach statistical significance, although LOS patients reported more adverse effects and better functional recovery. (Table 4) examines the impact of age at onset on prognosis and progression of schizophrenia. It shows that the time to first relapse is significantly shorter for EOS compared to LOS (10 months vs. 16 months, P-value=0.003). EOS patients also have a higher severity of symptoms at presentation and greater progression to severe disease (73.3% vs. 40%, P-value <0.001). The long-term functional outcomes are poorer for EOS patients (P-value=0.003) and there is a lower overall survival rate over five years compared to LOS (86.7% vs. 96.7%, P-value=0.043).

The data presented in Table 1 aligns with findings from existing studies showing that early-onset schizophrenia (EOS) is often characterized by more severe clinical features such as higher rates of auditory hallucinations, delusions, and negative symptoms compared to late-onset schizophrenia (LOS) Joslyn[8]. The pronounced cognitive decline in EOS (58.3% vs. 36.7%, P=0.009) supports research suggesting that earlier onset is associated with greater disruption in neuro developmental processes Karson[9]. Although the response to standard anti psychotics was higher in EOS, it was not significantly different (P=0.084), reflecting variability in treatment response documented in other studies Lally[10]. The findings in (Table 2), where EOS patients exhibited lower rates of visual hallucinations but higher rates of disorganized speech and social withdrawal, highlight the subtype differences that can influence clinical management strategies D'Antona[11]. The significant presence of paranoid delusions in LOS (P=0.006) supports literature that suggests a paranoia predilection in later life schizophrenia Tunvirachaisakul[12]. This differential pattern underlines the necessity for age-tailored diagnostic and therapeutic approaches, as also seen in studies by Chen[13]. As shown in (Table 3), LOS patients had a higher remission rate and fewer adverse effects from medication, though these findings were not statistically significant (P>0.05). The significantly higher

need for hospitalization and relapse rates in EOS (P<0.003 for both) corroborate with broader research indicating that earlier-onset patients may have a more chronic and debilitating course Fransen[14]. This suggests the importance of intensive early intervention programs which have been emphasized in other literature Hoftman[15]. (Table 4) reveals significant differences in the prognosis and progression of schizophrenia based on the age at onset. EOS patients faced a more rapid progression to severe disease and poorer long-term functional outcomes, aligning with studies suggesting worse prognostic outcomes for those with an earlier onset Puig[16]. The findings concerning overall survival and severity of symptoms at presentation offer insights into the progressive nature of schizophrenia when onset occurs early, necessitating a different management approach Collaborative[17].

CONCLUSION

This comparative study on Early-Onset Schizophrenia (EOS) versus Late-Onset Schizophrenia (LOS) has elucidated several crucial distinctions in clinical features and treatment outcomes between the two subtypes. Our findings underscore the more severe symptomatology and poorer prognosis associated with EOS compared to LOS. Specifically, EOS is characterized by a higher prevalence of auditory hallucinations, delusions, cognitive decline and negative symptoms. These features not only manifest more aggressively but also respond differently to treatment when compared to their later-onset counterparts. Our analysis revealed that while EOS patients generally exhibit a more severe clinical profile, they also face a more challenging treatment landscape. Despite a slightly higher response rate to standard anti psychotic treatments, the overall treatment outcomes for EOS, including relapse rates and the need for hospitalization, are less favorable than for LOS. Furthermore, LOS patients, although presenting later in life with a somewhat milder symptomatology, particularly marked by higher occurrences of paranoid delusions and visual hallucinations, tend to achieve better remission rates and experience fewer hospitalizations. The prognostic implications of our findings are significant, suggesting that age at onset should be a crucial consideration in the diagnostic and therapeutic processes for schizophrenia. Early-onset patients require a robust, tailored approach that addresses the severe and pervasive nature of their symptoms and their overall lower response to traditional treatment regimens. Conversely, treatment strategies for late-onset patients can be optimized by focusing on managing paranoia and improving functional outcomes, which appear to be more achievable in this group. In summary, this study highlights the necessity for differential diagnostic criteria and customized treatment plans that are sensitive to the age of onset in schizophrenia. Understanding these differences is vital for developing targeted interventions that can enhance quality of life and functional outcomes for all schizophrenia patients, irrespective of the age at onset. Future research should continue to explore the underlying biological, neurological and environmental factors that contribute to these disparities, aiming to refine treatment approaches and improve the prognosis for schizophrenia across the life span.

Limitations of Study:

- **Retrospective Design:** One of the main limitations of this study is its retrospective nature. Relying on historical medical records may introduce biases related to the accuracy and completeness of documented information. Moreover, changes in diagnostic criteria and treatment approaches over time can affect the consistency and reliability of the data collected.
- **Sample Size and Generalizability:** Although the study included 120 patients, this sample size may still be too small to capture the full variability of schizophrenia's clinical presentation, particularly within subgroups defined by age at onset. The findings from this study might not be generalizable to all populations, as the sample may not sufficiently represent diverse demographic backgrounds including different ethnicities, socioeconomic statuses, or healthcare access levels.
- **Lack of Longitudinal Follow-Up:** The absence of longitudinal follow-up restricts our understanding of the long-term progression and treatment response in patients. Longitudinal data would allow for a more dynamic observation of how clinical features evolve and how treatment responses may change over time, providing deeper insights into the chronic nature of schizophrenia.
- **Potential for Confounding Variables:** This study may also be limited by uncontrolled confounding factors that could influence both the onset of schizophrenia and the response to treatment. Factors such as genetic predispositions, environmental exposures and comorbid conditions were not comprehensively controlled for, which could skew the results and interpretations of the differences between EOS and LOS.
- **Diagnostic Accuracy:** The reliance on clinical diagnoses made at different points in time, potentially under varying diagnostic standards, poses a significant limitation. The accuracy and consistency of schizophrenia diagnoses,

particularly distinguishing between EOS and LOS, can vary considerably, influencing the study's findings.

- **Treatment Variability:** Treatment regimens were not standardized across the study cohort, which introduces variability in treatment outcomes. Differences in medication types, dosages and adjunct therapies could significantly impact the results, making it difficult to isolate the effects of age at onset from those of treatment strategies.
- **Specificity of Clinical Features:** The study broadly categorized clinical features and outcomes without delving into the specific symptoms or severity levels experienced by the patients. This generalization may overlook nuanced differences in symptomatology between EOS and LOS, potentially obscuring specific clinical insights.
- **Selection Bias:** Since the study was conducted at tertiary care hospitals, there may be a selection bias towards more severe cases or those with access to specialized care, which might not represent the broader population of individuals with schizophrenia.

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