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ORIGINAL ARTICLE

Comparative Evaluation of Diagnostic Challenges and Long-Term Outcomes in Early-Onset Schizophrenia

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ABSTRACT

Background: Early-onset schizophrenia (EOS), defined by psychotic symptom onset before 18 years of age, is associated with a more severe clinical trajectory and presents unique diagnostic and therapeutic challenges. Compared to adult-onset schizophrenia (AOS), EOS patients often experience delayed diagnosis, higher relapse rates, and poorer functional outcomes, especially in low-resource settings like Pakistan where early psychiatric symptoms are frequently underrecognized.

Aims and Objectives: This study aimed to compare the diagnostic challenges and long-term clinical and functional outcomes between EOS and AOS, and to identify predictors of poor prognosis in EOS patients to inform early intervention strategies.

Methodology: This was a retrospective comparative clinical study conducted at Sir Ganga Ram and Services Hospital, Lahore, from June 2022 to May 2023. A total of n=70 patients diagnosed with schizophrenia per DSM-5 criteria were divided equally into EOS (n=35) and AOS (n=35) groups. Data were collected on sociodemographic, symptom severity (PANSS), functional status (GAF), treatment delays, relapse rates, and hospitalizations. Logistic regression was performed to determine predictors of poor functional outcomes in EOS.

Results: EOS patients had significantly longer duration of untreated psychosis (p=0.002), higher PANSS scores (p=0.01), more relapses and hospitalizations (p<0.001), and lower GAF scores (p<0.001) compared to AOS. Predictors of poor outcomes included prolonged DUP (OR=1.25), lower education (OR=0.88), and lower socioeconomic status (OR=0.95).

Conclusion: EOS is associated with worse clinical and functional outcomes than AOS, driven by diagnostic delays and sociodemographic disadvantages. Early detection and targeted interventions are crucial to improve long-term prognosis in this vulnerable population.

Keywords: Early-Onset Schizophrenia, Adult-Onset Schizophrenia, Diagnostic Challenges, Duration of Untreated Psychosis, Prognosis, Functional Outcomes.

INTRODUCTION

Early-onset schizophrenia (EOS), characterized by the onset of psychotic symptoms occurring before age 18, is a clinical and research challenge because of its unique developmental and neurobiological features[1]. Schizophrenia affects approximately 1% of the population globally, and although only a small proportion of cases are early onset, research suggests that almost 15 to 25 percent of individuals with schizophrenia have symptom onset during adolescence. Differences in clinical practice and cultural factors result in different data estimates of the incidence of EOS, but worldwide data indicate that EOS has a notably lower incidence than adult-onset schizophrenia, and these cases often have a more severe clinical course, a longer duration of untreated psychosis, and more complex treatment needs[2].

In the context of epidemiological assessments, regions around the world report similar challenges with early detection and intervention. Such studies from Europe and North America have repeatedly shown that delayed diagnosis is associated with poorer long-term outcomes such as more frequent relapses, less recovery function, and greater psychosocial impairment. On the other hand, in areas with a well-developed early intervention program, there has been improvement in prognosis when timely and targeted therapeutic measures are used[3].

Epidemiological data within Pakistan indicate prevalence rates for schizophrenia of 1.0% to 1.5% for the general population. Although there are few data on EOS, as a result of underreporting and lack of distinction from other developmental and behavioural disorders, preliminary data suggest that approximately 10 to 20 percent of schizophrenia cases manifest before 18 years of age. These estimates highlight the importance of robust diagnostic protocols and frameworks for early intervention that recognize the developmental peculiarities of pediatric populations. All of this further adds to the challenges in Pakistan, where there is variable access to mental health services, under recognition of early psychiatric symptoms, and a lack of specialized child and adolescent psychiatry services[4, 5].

This present study was a comparative clinical investigation aimed at exploring the diagnostic challenges and long-term prognostic outcome of EOS compared to adult-onset schizophrenia (AOS). This study will contribute robust evidence towards improvements in early detection and personalized treatment strategies by systematically evaluating clinical presentations, duration of untreated psychosis, treatment modalities, and functional outcomes over a long period of follow-up[6]. This integration of worldwide statistics with region-specific data creates a broad framework to elucidate how different methods of diagnosis and models of intervention affect patient outcomes and consequently the need for a shift in paradigm relating to more efficient and effective mental health services for young people with psychosis[7, 8].

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MATERIALS AND METHODS

Study Design and Setting: The purpose of this comparative study was to investigate diagnostic challenges and long-term clinical outcomes of early-onset schizophrenia (EOS) versus adult-onset schizophrenia (AOS). The research was carried out at Sir Ganga Ram Hospital and Services Hospital Lahore, Pakistan, during a period of one year from June 2022 to May 2023. The objective of the study was to collect comprehensive data from patient records maintained at these tertiary care centers.

Participants and Sample Size: Overall, 70 patients were included in this investigation and were categorized into two separate groups depending on the age at onset of psychotic symptoms. Patients of the EOS group were classified as having symptom onset before 18 years of age; patients in the AOS group started with an episode of

psychosis at 18 years of age or older. Experienced psychiatrists confirmed all diagnoses by DSM-5 criteria.

Inclusion and Exclusion Criteria: Inclusion criteria for patients included a confirmed DSM-5 diagnosis of schizophrenia, adequate documentation of symptom onset, and clinical progression. For the AOS group, symptom onset at or after 18 years of age was necessary, and for the EOS group, symptom onset before the age of 18 was required. In addition, only patients with complete clinical records and a documented follow-up period of more than 5 years were included. Patients were excluded if they had comorbid neurological disorders or severe intellectual disabilities that would make it impossible to interpret the clinical findings, or if psychotic symptoms could be attributed to secondary causes, such as substance use or other medical conditions.

Data Collection Procedures: A systematic retrospective review of all medical records from the two participating hospitals was performed for patient data. A standardized data collection form was used to extract information on demographics, age at onset, clinical presentation, duration of untreated psychosis (DUP), treatment modalities, and functional outcomes. Two independent clinicians cross-verified data from the study period to ensure consistency and accuracy.

Clinical Assessments and Outcome Measures: Symptom severity and functional outcomes were first evaluated using validated diagnostic instruments in clinical assessments. We determined the duration of untreated psychosis as the time from the onset of psychotic symptoms to the start of appropriate therapeutic interventions. Instrumental measures of symptom severity (e.g., Positive and Negative Syndrome Scale, PANSS) and global functional outcome (e.g., Global Assessment of Functioning score, GAF) were systematically used to measure the severity of symptoms and overall functional outcomes. They permitted sufficient comparison of treatment efficacy, relapse frequency, and social, educational, and occupational functioning between the two groups.

Power Analysis: A power analysis was performed using a preliminary sample for the EOS and AOS groups to determine the appropriate sample size to detect statistically significant differences between the two groups. The sample size of 70 patients was deemed sufficient based upon expected effect sizes derived from previous literature regarding key outcome measures, including difference in the duration of untreated psychosis and functional outcomes, and an alpha level of 0.05, and a target power of 80%. This calculation ensured adequate power in the study to detect clinically meaningful differences between the groups and thus to strengthen the reliability and validity of the findings.

Statistical Analysis: SPSS software (version 25) was used for statistical analysis. Demographic and clinical characteristics of the entire sample were generated to describe descriptive statistics. Independent samples t-tests or nonparametric alternatives were used for the comparative analyses of continuous variables according to the distribution of the data, and categorical variables were compared using chi-square tests. Potential predictors of long-term functional outcomes in the EOS group were sought through logistic regression analysis. All tests were conducted at the significance level of p-value less than 0.05.

Ethical Considerations: The study was conducted as per the ethical guidelines governing research with human subjects. Before the commencement of study, the institutional review boards of Sir Ganga Ram Hospital, Lahore, and Services Hospital, Lahore, approved. Since the chart review was retrospective, the study was granted a waiver of informed consent. Access to sensitive information was authorized only in case of authorized personnel, and patient records were de-identified to maintain confidentiality. The study was carried out in compliance with the principles of the Declaration of Helsinki and the protection of the rights and well-being of the participants.

RESULTS

A total of 70 patients were included in the analysis: 35 with EOS (onset < 18 years) and 35 with AOS (onset ≥ 18 years). In addition, a large number of demographic variables were recorded to further describe the patient profiles in both cohorts. The demographic markers included age at onset, gender, educational attainment, employment status, marital status, residence (urban vs. rural), socioeconomic status, and family history of psychiatric illness.

Demographic Characteristics: The mean age at onset of the EOS group was 16.1 ± 1.3 years, which was significantly less than the AOS group (mean age at onset 24.5 ± 4.2 years, $p < 0.001$). There was no difference between the two groups in gender distribution (EOS: 57.1% males vs. AOS: 51.4% males, $p = 0.73$). The EOS patients were surprisingly also less educated, with an average of 9.2 ± 3.1 years of schooling compared to 11.8 ± 2.6 years in the AOS group ($p = 0.001$). Employment status was different too: only 22.9% of EOS patients were employed full time compared with 45.7% of AOS patients ($p = 0.02$). Lastly, there was a significant difference seen in marital status, with only 28.6% of EOS patients being married compared to 51.4% of AOS patients ($p = 0.04$). Regarding residence, the percentage of EOS patients and AOS patients living in urban areas was 85.7% and 82.9% ($p = 0.67$). Consistent with the lower socioeconomic status, the EOS group (mean composite index score: 42.3 ± 8.5) had a significantly poorer socioeconomic status compared to the AOS group (mean composite index score: 50.1 ± 7.2; $p = 0.003$). In addition, 45.7% of EOS patients, but only 34.3% of AOS patients, had a family history of psychiatric illness, though this did not reach statistical significance ($p = 0.33$).

Table 1: Expanded Demographic and Baseline Clinical Characteristics

Variable	EOS (n = 35)	AOS (n = 35)	p-value
Age at Onset (years)	16.1 ± 1.3	24.5 ± 4.2	< 0.001
Gender (Male: Female)	20:15	18:17	0.73
Years of Education	9.2 ± 3.1	11.8 ± 2.6	0.001
Employment Status (% Employed)	8 (22.9%)	16 (45.7%)	0.02
Marital Status (% Married)	10 (28.6%)	18 (51.4%)	0.04
Residence (Urban/Rural)	30 (85.7%)/5 (14.3%)	29 (82.9%)/6 (17.1%)	0.67
Socioeconomic Status (Index Score)	42.3 ± 8.5	50.1 ± 7.2	0.003
Family History of Psychiatric Illness (%)	16 (45.7%)	12 (34.3%)	0.33

Table 2: Long-Term Clinical and Functional Outcome Measures

Outcome Variable	EOS (n = 35)	AOS (n = 35)	p-value
Duration of Untreated Psychosis (weeks)	14.7 ± 4.8	10.5 ± 3.2	0.002
Baseline PANSS Score	90.3 ± 7.5	85.2 ± 8.3	0.01
GAF Score at Follow-Up	45.2 ± 9.7	55.8 ± 7.6	< 0.001
Number of Relapses	2.4 ± 1.1	1.3 ± 0.8	< 0.001
Number of Hospitalizations	1.8 ± 0.9	1.2 ± 0.5	0.001

Clinical Characteristics and Long-Term Outcomes: The two groups were found to be significantly different in clinical assessments. The mean DUP was 14.7 ± 4.8 weeks in the EOS patients vs 10.5 ± 3.2 weeks in the AOS patients ($p = 0.002$). The EOS group (90.3 ± 7.5) had higher baseline symptom severity ($p = 0.01$) than the AOS group (85.2 ± 8.3). Functional outcomes as assessed by the Global Assessment of Functioning (GAF) score were significantly worse over the follow-up period, which was at least 5 years, in EOS patients (45.2 ± 9.7) than AOS patients (55.8 ± 7.6, $p < 0.001$). In addition, clinical relapses and hospitalizations were markedly increased among the EOS group compared with the AOS group (2.4 ± 1.1 relapses, 1.8 ± 0.9 hospitalizations vs 1.3 ± 0.8 relapses, 1.2 ± 0.5 hospitalizations; $p < 0.001$ and $p = 0.001$, respectively).

Multivariable Analysis of Predictors for Poor Functional Outcome: To examine the predictors of poor long-term functional outcomes, a logistic regression model was generated from the EOS cohort with a poor long-term functional outcome (GAF score

below 50). The independent variables were duration of untreated psychosis (DUP), years of education, and socioeconomic status. The model showed that an extended DUP was significantly related to poor outcomes (OR = 1.25, 95% CI: 1.05–1.49; p = 0.01). In addition, each additional year of education decreased risk of a poor outcome (OR = 0.88, 95% CI = 0.80–0.97, p = 0.008), and a higher socioeconomic status was protective (OR = 0.95 per unit increase in index score, 95% CI = 0.91–0.99, p = 0.02).

Table 3: Logistic Regression Analysis for Predictors of Poor Outcome (GAF < 50) in EOS

Predictor	Odds Ratio (OR)	95% Confidence Interval	p-value
Duration of Untreated Psychosis (weeks)	1.25	1.05–1.49	0.01
Years of Education	0.88	0.80–0.97	0.008
Socioeconomic Status (per unit score)	0.95	0.91–0.99	0.02

Therefore, in summary, the comparative analysis showed that patients have early-onset schizophrenia with a lower age at onset, poorer educational outcomes, lower socioeconomic status, and lower rates of employment and marriage. Consistent with these sociodemographic disadvantages, the duration of untreated psychosis and baseline symptom severity were longer. In the long term, EOS patients had notably worse functional outcomes than adult-onset patients, as demonstrated by lower GAF scores, higher relapse rates, and increased hospitalizations. In the EOS cohort, prolonged DUP, lower educational attainment, and lower socioeconomic index were significant predictors of adverse long-term outcomes in the multivariable analysis.

These data underscore the importance of early diagnosis and early, tailored intervention in patients with early-onset schizophrenia to prevent the long-term functional impairments and improve the quality of life of this population.

DISCUSSION

In this study, the differences between early-onset schizophrenia (EOS) and adult-onset schizophrenia (AOS) in terms of demographic profiles, clinical severity, and long-term functional outcomes are compared comprehensively. The findings reinforce that schizophrenia at an earlier age is a unique clinical challenge to diagnose and treat[9]. Besides the considerably lower age at onset, patients in the EOS group are burdened by a series of sociodemographic disadvantages: lower educational attainment, lower socioeconomic status, lower employment and marital rates. Worse long-term prognoses relative to their AOS counterparts are also observed for these factors, as well as for a prolonged duration of untreated psychosis (DUP) and higher baseline symptom severity[10].

The observation of the extended DUP among EOS patients is particularly notable. Repeatedly associated with increased chronicity of symptoms and diminished response to therapeutic interventions are delays in initiating treatment. These findings are supported by our study, which found that EOS patients had markedly higher relapse rates, more frequent hospitalizations, and lower Global Assessment of Functioning (GAF) scores over the five-year follow-up period [11]. Based on this data, early psychotic episodes—occurring at critical periods of neurodevelopment—may disrupt the progression of neurodevelopmental processes, resulting in persistent deficits in cognitive, social, and occupational domains of functioning. On the other hand, the relatively lower DUP in AOS patients has a more favorable outcome and suggests that earlier access to care could prevent the long-term adverse effects of the disorder [12].

A major contribution of our findings is the link between unfavorable socioeconomic status and lower educational levels with adverse outcomes in the EOS population. These sociodemographics are likely to exacerbate the inherent difficulties of early-onset psychosis. Preexisting vulnerabilities and lower educational attainment and socioeconomic status may not only be a reflection, but may also establish and perpetuate a cycle of disadvantage where treatment adherence, access to resources, and overall quality of life are diminished[13]. The logistic regression confirmed that each additional week of untreated psychosis increased the odds of a poor outcome and that each additional year of education reduced the risk. This complexity of the interplay between the clinical and sociodemographic variables reflects the need for an integrated approach to treatment that considers both the psychiatric and broader social determinants of health [14].

Additionally, the higher baseline PANSS scores in the EOS group indicate a more aggressive clinical trajectory of schizophrenia when it occurs during adolescence. This is in agreement with the notion that the neurodevelopmental aberrations of EOS constitute a more global and drug-resistant form of the disorder[15]. In addition, the greater frequency of relapses and hospitalizations in the EOS group suggests a clinical instability pattern that can be associated with profound effects on long-term functional outcomes. Therefore, this instability requires that we reevaluate current intervention strategies for early detection, rapid treatment initiation, and long-term support[16].

This has important clinical implications. First, it emphasizes the need to refine diagnostic criteria and build robust screening protocols to identify psychosis at its earliest stages. Public health initiatives, mental health education, and integration of early intervention services in primary and secondary care settings should be a critical focus to reduce the duration of untreated psychosis. Second, the sociodemographic disparities that adversely affect patients with EOS should be addressed. Some of the negative effects of low socioeconomic status and limited educational opportunities can be mitigated to some extent with multidisciplinary interventions that combine psychoeducation, vocational training, and social support[17, 18].

However, the study has certain limitations. However, retrospective design is valuable for evaluating long-term outcomes, however, recall bias is inherent to record review. Furthermore, although our sample size was calculated a priori using power analysis, the small number of patients may preclude the generalizability of our results[19]. These results need to be validated by subsequent future prospective studies with larger, more diverse samples to further explore the mechanisms underlying the differential trajectories of early onset versus adult onset schizophrenia[20].

CONCLUSION

These results indicate that patients with early-onset schizophrenia present a more difficult clinical course and worse long-term outcome compared to those with adult-onset schizophrenia. Because patients in the EOS group have an extended duration of untreated psychosis, greater baseline symptom severity, and significant socioeconomic disadvantages, they have higher relapse rates, more hospitalizations, and lower functional capacity over time. These findings reinforce the importance of early detection and appropriate intervention designed for the individualized developmental and clinical features of young patients with schizophrenia. What must be done is not only to treat the psychiatric symptoms, but also to address the larger social and economic determinants that affect long-term outcomes. Enhancements in early-onset schizophrenia quality of care and prognosis require improved diagnostic protocols, comprehensive early intervention programs, and policies such as mitigating socioeconomic disparities.

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