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Neurological Soft Signs and Functional Impairment in First-Episode Schizophrenia: Association with Duration of Untreated Illness

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ABSTRACT

Background: Neurological soft signs (NSS) are subtle abnormalities in motor coordination, sensory integration, and complex motor sequencing commonly observed in schizophrenia. They are considered potential markers of neurodevelopmental abnormalities and may be associated with illness severity and functional outcomes. This study examined the association between NSS, global functioning, and duration of untreated illness in patients with first-episode schizophrenia with minimal prior antipsychotic exposure.

Methods: This cross-sectional study included 60 patients diagnosed with schizophrenia according to ICD-10 criteria attending a tertiary care teaching hospital. Neurological soft signs were assessed using the Neurological Evaluation Scale (NES), while functional status was evaluated using the Global Assessment of Functioning (GAF) scale. Duration of illness was categorized into four groups (1–3 months, 4–6 months, 7–12 months, and ≥12 months). Associations between variables were analyzed using the Fisher–Freeman–Halton exact test.

Results: Longer duration of illness was significantly associated with a greater burden of neurological soft signs (p=0.001). Patients with shorter illness duration predominantly demonstrated fewer neurological soft signs, whereas higher NSS counts were observed among those with longer illness duration. Neurological soft signs were also significantly associated with poorer global functioning (p=0.001), with higher NSS counts corresponding to lower GAF scores.

Conclusion: Neurological soft signs are significantly associated with longer duration of untreated illness and poorer global functioning in first-episode schizophrenia. These findings support the potential role of NSS as clinically relevant markers of illness severity and functional impairment during the early stages of schizophrenia.

Key-words: Schizophrenia; Neurological Soft Signs; Neurological Evaluation Scale; Global Assessment of Functioning; First-Episode Psychosis; Functional Outcome

INTRODUCTION

Schizophrenia is a chronic and severe psychiatric disorder affecting approximately 1% of the global population and remains one of the leading causes of disability among young adults worldwide.

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It is characterized by disturbances in thought, perception, affect, cognition, and behavior, resulting in substantial impairment in social and occupational functioning [1,2].

Although positive symptoms such as hallucinations and delusions are often the most clinically apparent manifestations of schizophrenia, increasing evidence suggests that neurological abnormalities and functional impairments represent core features of the disorder [3,4]. Among these abnormalities, neurological soft signs (NSS) have emerged as important markers of altered neurodevelopment and aberrant brain connectivity [5].

Neurological soft signs are subtle, non-localizing neurological abnormalities involving motor coordination,

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sensory integration, sequencing of complex motor acts, and inhibitory control [6]. Unlike focal neurological deficits, NSS do not correspond to discrete structural lesions but are thought to reflect dysfunction within distributed neural networks involving fronto-cerebellar, thalamo-cortical, and cortico-subcortical circuits [7,8].

Meta-analytic evidence consistently demonstrates significantly higher rates of NSS among patients with schizophrenia compared with healthy controls and individuals with other psychiatric disorders [9,10]. Importantly, NSS have been observed in antipsychotic-naïve individuals, first-degree relatives of patients with schizophrenia, and individuals at clinical high risk for psychosis, suggesting that these abnormalities may represent trait markers of vulnerability rather than consequences of illness chronicity or pharmacological treatment [11–13].

Functional impairment remains one of the most disabling consequences of schizophrenia. Even during early stages of illness, many patients experience substantial difficulties in maintaining educational attainment, employment, interpersonal relationships, and independent living [14]. Previous studies have demonstrated that neurological abnormalities are associated with poorer psychosocial functioning, reduced quality of life, and worse long-term outcomes [15,16].

Duration of untreated illness (DUI) and duration of untreated psychosis (DUP) have emerged as critical predictors of clinical outcomes in schizophrenia. Longer delays in treatment initiation have been associated with increased symptom severity, poorer treatment response, cognitive deterioration, and greater functional disability [17,18]. However, the relationship between untreated illness duration and neurological soft signs remains incompletely understood, particularly in first-episode patients with minimal antipsychotic exposure.

Studies involving first-episode schizophrenia are of particular importance because they allow assessment of illness-related abnormalities before the confounding effects of prolonged disease progression and long-term antipsychotic treatment become prominent [19]. Investigating NSS in this population may improve understanding of schizophrenia pathophysiology and identify clinically useful markers associated with functional outcomes.

The present study therefore aimed to examine the relationship between neurological soft signs, global functioning, and duration of untreated illness among patients with first-episode schizophrenia.

Inclusion Criteria

- Age between 18 and 60 years.
- Diagnosis of schizophrenia according to ICD-10 criteria.
- First-episode illness.
- Less than one month of prior antipsychotic exposure.
- Ability to provide informed consent.
- Ability to understand Hindi or English.

Exclusion Criteria

- Comorbid psychiatric disorders.
- Substance intoxication or withdrawal states.
- Organic mental disorders.
- Significant neurological or medical illnesses affecting assessment.
- Refusal to participate.

Assessments

Neurological Evaluation Scale (NES)- Neurological soft signs were assessed using the Neurological Evaluation Scale, a standardized instrument evaluating sensory integration, motor coordination, sequencing of complex motor acts, and related neurological abnormalities.

Global Assessment of Functioning (GAF)- Overall psychological, social, and occupational functioning was assessed using the Global Assessment of Functioning scale.

Duration of Illness- Duration of illness was determined through clinical interviews and collateral information and categorized as:

- 1–3 months
- 4–6 months
- 7–12 months
- ≥12 months

Statistical Analysis- Data were analyzed using IBM SPSS Statistics version 23. Descriptive statistics were calculated for demographic and clinical variables. Associations between duration of illness, neurological soft signs, and GAF scores were examined using the

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Fisher–Freeman–Halton exact test. Statistical significance was set at $p < 0.05$.

RESULTS

A total of 60 patients with first-episode schizophrenia were included in the study. The majority of participants had a duration of illness between 7 and 12 months (53.3%, n=32), followed by 4–6 months (28.3%, n=17) and 1–3 months (16.7%, n=10). Only one participant had an illness duration of 12 months or longer (1.7%, n=1) (Table 1).

Table 1: Distribution of Duration of Illness (N = 60)

Duration of illness	n	%
1–3 months	10	16.7
4–6 months	17	28.3
7–12 months	32	53.3
≥12 months	1	1.7
Total	60	100

Regarding global functioning, most patients demonstrated substantial impairment. Twenty-four participants (40.0%) had GAF scores between 21 and 30, indicating behavior considerably influenced by delusions or hallucinations or serious impairment in communication or judgment. Seventeen patients (28.3%) had GAF scores between 41 and 50, while 14 (23.3%) had scores between 11 and 20. Only three participants (5.0%) had GAF scores between 51 and 60 and two (3.3%) scored between 31 and 40 (Table 2).

Table 2: Distribution of Functional Impairment According to GAF Scores (N = 60)

GAF Category	n	%
51–60	3	5.0
41–50	17	28.3
31–40	2	3.3
21–30	24	40.0
11–20	14	23.3
Total	60	100

A statistically significant association was observed between duration of illness and neurological soft signs (Fisher–Freeman–Halton Exact Test, p=0.001). Patients with shorter illness duration predominantly exhibited lower NSS counts, whereas those with longer illness duration demonstrated progressively higher NSS burden. Among patients with illness duration of 1–3 months, 90% had fewer than three neurological soft signs. In contrast, patients with illness duration of 7–12 months predominantly demonstrated five or more neurological soft signs. The single patient with illness duration ≥12 months exhibited nine neurological soft signs (Table 3).

Table 3: Association between Duration of Illness and Neurological Soft Signs

Duration of Illness	NSS 0–2	NSS 3–5	NSS ≥6	Total
1–3 months	9	1	0	10
4–6 months	14	0	3	17
7–12 months	1	7	24	32
≥12 months	0	0	1	1
Total	24	8	28	60

Fisher–Freeman–Halton Exact Test: p=0.001

Patients with illness duration exceeding six months demonstrated substantially greater NSS burden than those with shorter illness duration. Nearly three-fourths of patients in the 7–12 month group had six or more neurological soft signs, whereas none of the patients in the 1–3 month group demonstrated this level of neurological abnormality.

DISCUSSION

The present study examined the relationship between neurological soft signs, duration of untreated illness, and global functioning among patients with first-episode schizophrenia with minimal prior antipsychotic exposure. Two major findings emerged. First, longer duration of untreated illness was associated with a greater burden of neurological soft signs. Second, higher NSS burden was significantly associated with poorer global functioning.

Neurological soft signs have consistently been reported as one of the most robust neurological abnormalities observed in schizophrenia. A recent systematic review by Zhao et al. reported significantly elevated NSS prevalence in first-episode schizophrenia compared with healthy controls, supporting the hypothesis that NSS represent core neurodevelopmental manifestations of the disorder rather than secondary consequences of chronic illness [20]. Our findings are consistent with this interpretation.

The observed association between longer illness duration and increased NSS burden is clinically

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important. Previous investigations have demonstrated that delayed treatment initiation is associated with worsening psychopathology, reduced recovery rates, and poorer functional outcomes [17,21]. The higher frequency of neurological abnormalities observed among patients with longer untreated illness may reflect progressive disruption of neural connectivity or increasing clinical expression of underlying neurodevelopmental abnormalities.

Several neuroimaging studies provide biological support for this interpretation. Structural and functional abnormalities involving the cerebellum, thalamus, basal ganglia, and prefrontal cortex have been linked to NSS severity in schizophrenia [22,23]. Diffusion tensor imaging studies have further demonstrated white matter abnormalities within fronto-cerebellar networks among individuals exhibiting prominent NSS [24].

The significant inverse association between NSS burden and GAF scores observed in the present study supports previous findings linking neurological abnormalities with impaired psychosocial functioning. Galderisi *et al.* reported that neurological and cognitive impairments contribute substantially to functional disability beyond the effects of positive symptoms alone [25]. Similarly, Harvey and Strassnig demonstrated that neurological and neurocognitive abnormalities are among the strongest predictors of real-world functioning in schizophrenia [26].

Our findings support the growing view that NSS may represent clinically meaningful indicators of illness severity rather than merely ancillary neurological observations. Early identification of patients with high NSS burden may facilitate targeted rehabilitation interventions and closer monitoring of functional outcomes [27,28].

The present study possesses several strengths. First, the inclusion of first-episode patients with minimal antipsychotic exposure reduced potential confounding by medication-related motor abnormalities. Second, standardized assessment instruments were employed to evaluate neurological abnormalities and functioning. Third, the study contributes data from an Indian population, which remains underrepresented in the international literature [29,30].

LIMITATIONS

Several limitations should be considered. The cross-sectional design precludes causal inferences regarding the relationship between NSS and illness duration. The study was conducted at a single tertiary care center and involved a relatively modest sample size. In addition, the absence of a healthy control group limits direct comparisons with normative populations. Future longitudinal studies incorporating neuroimaging and functional outcome measures are needed to clarify the temporal relationship between neurological abnormalities and disease progression.

CONCLUSIONS

Neurological soft signs were significantly associated with both longer duration of untreated illness and poorer global functioning among patients with first-episode schizophrenia. Patients with prolonged untreated illness demonstrated a substantially greater burden of neurological abnormalities, while higher NSS scores were associated with lower levels of psychosocial functioning. These findings support the hypothesis that neurological soft signs represent clinically meaningful markers of neurodevelopmental dysfunction and illness severity in schizophrenia. Early identification of NSS may facilitate timely intervention, improved treatment planning, and closer monitoring of functional outcomes. Longitudinal studies with larger samples are warranted to further clarify the prognostic significance of neurological soft signs during the early course of schizophrenia.

CONTRIBUTION OF AUTHORS

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