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**ORIGINAL PAPER:**

# FREQUENCY AND ASSOCIATION OF COGNITIVE DYSFUNCTION IN SCHIZOPHRENIA: A CROSS-SECTIONAL STUDY FROM A TERTIARY CARE HOSPITAL IN PAKISTAN

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**ABSTRACT**

**OBJECTIVE**

To assess the frequency of cognitive impairment and sociodemographic association among patients with schizophrenia presenting to a tertiary care hospital in Pakistan.

**STUDY DESIGN**

Descriptive cross-sectional study

**PLACE AND DURATION OF STUDY**

Outpatient Department of Psychiatry at Dr Ruth K.M. Pfau. Civil Hospital Karachi, Pakistan. The duration of the study was 6 months from February 6, 2020, to August 5, 2020.

**METHOD**

One hundred thirty patients with schizophrenia were assessed using the Urdu version of Montreal cognitive assessment questionnaire.

**RESULTS**

out of the 100 patients, 66 had significant cognitive impairment accounting for more than half of the study population at 50.8%. Age, duration of illness and gender showed significant association with cognitive dysfunction in these patients.

**CONCLUSION**

Cognitive dysfunction is a frequent finding in patients with schizophrenia. Future research is needed to investigate the factors increasing its risk.

**KEYWORDS**

Cognition; Memory; Outpatients; Pakistan; Schizophrenia; Tertiary Care Centres.

## INTRODUCTION

Originally termed as' dementia praecox' in 1896 by Kraepelin, and renamed in 1908 by Bleuler as schizophrenia [1], schizophrenia is a serious mental disorder that affects approximately 20 million individuals globally [2]. It is the third leading cause of morbidity among people aged between 15 and 44 in the world [3] and has been ascertained to account for 1.1% of the total disability adjusted life years worldwide and 2.8% of the years lived with disability worldwide. [4]

Cognitive impairment alludes to a decline in function in either one or several domains of cognitive function such as the ability to perform tasks in a selective and focused way, to concentrate over a span of time, to grasp new information and skills, to determine strategies

for actions and to execute them. [5] Although psychosis is usually the most striking clinical aspect of schizophrenia, recent research now shows that disturbances in certain cognitive processes, such as attention, certain types of memory, and executive functions, are the contributing features of the illness.[6]

Significant breakthrough has been made in understanding the biological basis of the disorder and important advances have been made in the management of positive symptoms, other serious areas, such as cognition and social cognition, are a neglected aspect of schizophrenia and have not been adequately addressed. Cognitive impairment has been estimated to be present in over 80% of patients with schizophrenia. Such cognitive disturbances can exist for years before the onset of psychosis and persist throughout the illness [7] non-pharmacological interventions such as cognitive remediation programs consistently show benefits and are part of the clinical guidelines [8]

The scarcity of data on cognitive deficits in patients with schizophrenia in Pakistan highlights a significant knowledge gap, underscoring the need for our study. This research aims to address this gap by estimating the prevalence of cognitive impairment in individuals with schizophrenia and exploring the sociodemographic factors that contribute to these deficits. Thus, this study aims to assess the frequency of cognitive impairment and sociodemographic association among patients with schizophrenia presenting to a tertiary care hospital in Pakistan.

## METHOD

After approval of FCPS dissertation synopsis from the College of Physicians and Surgeons Pakistan (REU-41997), and ethical approval from the Department of Psychiatry, Dr Ruth K.M. Pfau. Civil Hospital Karachi, Pakistan**,** a descriptive cross-sectional study was initiated at the Outpatient Department of Psychiatry, Dr Ruth K.M. Pfau. Civil Hospital Karachi, Pakistan, to determine the frequency of cognitive deficits in patients with schizophrenia. The period of the study was of six months from February 6, 2020, to August 5, 2020.

After taking appropriate consent from either the patient or their caregiver, the research was conducted and the sampling technique used was Non-Probability, Consecutive Sampling. The inclusion criteria of the study participants included both male and female genders, with aged between 18 and 60 years, diagnosed with schizophrenia as per DSM-5 criteria by the clinicians and had used anti-psychotic medication for at least 2 months.

Exclusion criteria included patients who suffered from chronic brain disease, who were diagnosed with any medical condition as per their medical record, those with substance use disorder, or who were unable to understand the procedure of the study.

A total of 130 patients were evaluated. The sample size was calculated by using Open Epi software, with confidence interval was 95%, margin of error 8% and prevalence of cognitive dysfunction in schizophrenia were seen in 70% [4].

**DATA COLLECTION**

After departmental approval, schizophrenia patients from Dr. Ruth K.M. Pfau Civil Hospital Karachi's outpatient clinic were screened and enrolled per inclusion criteria. Informed consent was obtained, ensuring confidentiality. Demographics, psychiatric history, and cognitive function (assessed via the Urdu Montreal Cognitive Assessment, score <26/30) were recorded. The frequency of cognitive dysfunction and its association with sociodemographic factors were analysed.

**DATA ANALYSIS**

Data analysis was conducted using SPSS version 20. Descriptive statistics calculated mean and standard deviation for age and schizophrenia duration, while frequencies and percentages were used for qualitative variables (e.g., gender, marital status, socioeconomic status, obesity, residence status, and cognitive dysfunction). Stratification controlled for effect modifiers, and a chi-square test were used to assessed the association of variable and their impact on the outcome. A p-value ≤ 0.05 was considered significant.

**RESULTS**

A total of 130 patients with schizophrenia were included in this study to assess their cognitive dysfunction presenting at a tertiary care hospital in Pakistan.Majority of the patients were males; 82 males (63.1%) while 48 (36.9%) were females. The age at presentation for schizophrenia ranged from 18 to above 40 years with the Mean ± SD of age being 33.38±11.69 with C.I (31.35-35.41) years. Out of the 130 patients assessed 69 (53.1%) were married while 61 (46.9%) were unmarried. Socioeconomic stratification showed that 39 (30%) patients belonged to the lower income group (income less than 15000), 54 (41.5%) were from middle income group (15000---35000) while 37 (28.5%) were from higher income group (an income greater than 35000).

The Mean ± SD for duration of having schizophrenia in these patients was 6.94±4.64 with C.I (6.13-7.74) years. Cognitive dysfunction was found to be in 66 (50.8%) patients.

In our study, stratification of confounders/effect modifiers with respect to cognitive dysfunction showed significant difference in age group (P=0.0001), duration of schizophrenia (P=0.0001), gender (P=0.002) whereas insignificant difference was noted in marital status (P=0.287), obesity (P=0.105), socioeconomic status (P=0.765) and residential status (P=0.383). (Table 1)

**Table 1**
**Demographic features of patients with and without cognitive dysfunction**

| Demographic Features | | Cognitive Dysfunction | | p- value |
|---|---|---|---|---|
| | | Yes | No | |
| **Age Group** | 18-40 | 42 (32.3%) | 60 (46.2%) | 0.0001 |
| | > 40 | 24 (18.5%) | 4 (3.1%) | |
| **Duration (In Years)** | 2 – 5 | 18 (13.8%) | 58 (44.6%) | 0.0001 |
| | > 5 | 48 (36.9%) | 6 (4.6%) | |
| **Gender** | Male | 16 (12.3%) | 32 (24.6%) | 0.002 |
| | Female | 50 (38.5%) | 32 (24.6%) | |
| **Marital Status** | Married | 32 (24.6%) | 37 (28.5%) | 0.287 |
| | Unmarried | 34 (26.2%) | 27 (20.8%) | |
| **Socio-Economic Status** | Lower Income | 20 (15.4%) | 19 (14.6%) | 0.765 |
| | Middle Income | 29 (22.3%) | 25 (19.2%) | |
| | Upper Income | 17 (13.1%) | 20 (15.4%) | |
| **Residential Status** | Urban | 47 (36.2%) | 41 (31.5%) | 0.383 |
| | Rural | 19 (14.6%) | 23 (17.7%) | |

## DISCUSSION

In the present study, frequency of cognitive dysfunction was found in 66 (50.8%) patients. Our finding is consistent with previous western studies, which stated the prevalence of cognitive deficits in schizophrenia from 75% to 83%. In one study, 75.7% of patients with schizophrenia had cognitive deficits based on ACE-III scores. Another study found that 77.7% of elderly patients with chronic schizophrenia had cognitive impairment.[9] Research on the topic is limited in Asian countries. Research from Nepal showed that the prevalence of working memory impairment in a sample of Nepalese antipsychotic-naïve patients with schizophrenia to be 86.7% [10]. Similarly, research published from Thailand documents cognitive impairment in 81.3% of the study sample when measured with the Montreal Cognitive Assessment Tool (MoCA-T) [11]. However, in both these studies, certain limitations appear as a small sample size of 30 and 81, respectively.

However, a multi-centre study, conducted in Japan with a representative sample of patients with schizophrenia, used the Adult Wechsler Adult Intelligence Scale III (WAIS-III) and estimated the cognitive dysfunction after the onset of schizophrenia to be 70% [12]. Another research conducted in China showed that the first episode and patients with chronic schizophrenia scored lower compared to the normal control [13].

Research from our Western counterparts shows an equally high prevalence [14]. Therefore, the findings of our study further reinforce the notion that cognitive impairment is an essential part of the illness.

The causation of cognitive impairment has been extensively researched with several hypotheses. One of these hypotheses is the neurodevelopment hypothesis. Earlier, neurogenesis or neuronal multiplication was restricted to intrauterine life and early childhood years; however, research now proves that the process of neurogenesis persists through adulthood to late life, although the process gets restricted to certain confined areas of the brain like the olfactory bulb, hippocampus, and periventricular areas [15,16].

Schizophrenia is believed to stem from abnormal neurodevelopment, and it is these abnormalities in neurodevelopment that may be culpable for the cognitive deficits in schizophrenia. However, this neurodevelopmental hypothesis has its limitations in explaining the extensive brain changes in schizophrenia, which can rather be explained as the cumulative effect of neurodevelopmental abnormality, change in neuroplasticity and alteration in neuronal maturation [17].

The core symptoms of schizophrenia, like negative symptoms and executive dysfunction, are the direct consequences of altered neuroplasticity. Brain derived neurotrophic factor (BDNF) is associated with the hippocampal neuroplasticity, which is involved in cognitive processing. Schizophrenia causes neurodevelopmental changes, which alter the BDNF mediated hippocampal neuroplasticity, attributing to the cognitive deficits [18].

It has been researched that neuronal glycoprotein M6a has a role in facilitating neurite outgrowth, synaptogenesis, and neuroplasticity. Patients with schizophrenia develop abnormal connections in the brain resulting from abnormal synaptic plasticity leading to dysconnectivity in brain neuronal network. Dysconnectivity due to abnormal synaptic plasticity, results in impairment of learning and information processing, which is manifested in the form of cognitive deficits in schizophrenia [19]

In our study, Cognitive dysfunction was found in 50.8% of patients with schizophrenia, highlighting its significant frequency and the need for its inclusion in comprehensive management plans. Younger patients, particularly those aged 18–40, were more likely to exhibit cognitive dysfunction (p=0.0001), which may be due to earlier onset and longer disease exposure. The duration of schizophrenia also played a critical role, with those having the illness for over 5 years showing a significantly higher likelihood of cognitive impairments (p=0.0001). Gender differences were notable, as females were disproportionately affected (p=0.002), warranting further exploration of underlying biological or psychosocial factors.

Interestingly, while a higher proportion of urban residents exhibited cognitive dysfunction, the difference was not statistically significant (p=0.383). These findings emphasize the importance of addressing modifiable and disease-related factors, such as the duration of illness and providing tailored interventions for at-risk groups, particularly females and younger individuals.

Apart from establishing the frequency of cognitive dysfunction in schizophrenia, our study also made significant association of cognitive deficits with certain demographic factors.

One limitation of this study is that it was conducted during the COVID-19 pandemic, where social isolation and reduced stimulation may have contributed to cognitive impairment. Additionally, the single centred setting in a public-sector hospital and the cross-sectional design limit the generalizability of our findings. Future studies should incorporate control groups, longitudinal designs to better differentiate pandemic-related effects and improve external validity.

**CONCLUSION**

From the findings of this study, it can be concluded that cognitive dysfunction is indeed a frequent finding in patients with schizophrenia in Asian countries as well and highlights the necessity of early identification of cognitive dysfunction for the effective management of schizophrenia

**RECOMMENDATIONS**

Our findings outline the need for future research to investigate those factors that could be considered as higher risk of cognitive dysfunction. Future prospective and more epidemiological studies that evaluate cognitive dysfunction among large sample size with multiple study centres in Pakistan are needed to confirm the findings of the present study

**CONFLICT OF INTEREST.**

The authors declare no competing interest.

**DISCLOSURE**

The study is based on an FCPS dissertation approved by the College of Physicians and Surgeons Pakistan on 30th September 2021.

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**AUTHOR(S) CONTRIBUTION/UNDERTAKING FORM**

| No. | Author Name | Author Affiliation | Contribution |
|---|---|---|---|
| 1 | Dr. Zainab Sher | Department of Psychiatry, Aga Khan University Pakistan | concept mapping, data analysis and interpretation of study findings, critically reviewed the manuscript |
| 2 | Dr. Fawad Suleman | Department of Psychiatry, Aga Khan University Pakistan | contributed to literature search of the study, worked on the initial draft and critically reviewed the manuscript |
| 3 | Dr. Samiya Iqbal | Department of Psychiatry, Aga Khan University Pakistan | contributed to literature search of the study, worked on the initial draft and critically reviewed the manuscript |
| 4 | Dr. Amber Tahir | Department of Psychiatry, Ruth Pfau Civil Hospital, Karachi | contributed to methodology of the study, critically reviewed the manuscript |
| 5 | Samia Rafi | Batterjee Medical College for Sciences and Technology, Jeddah, Saudi Arabia | worked on the initial draft of the manuscript |