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Original Article

Cognitive Deficits in Adult Schizophrenia and its Association with Clinical Factors

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ABSTRACT

Objective: To assess cognitive deficits, their severity and associated clinical factors in adult patients of Schizophrenia, and to compare them with controls in psychiatric setups of Gilgit and Rawalpindi.
Study Design: Comparative cross-sectional study.
Place and Duration of Study: Psychiatry Department, Combined Military Hospital, Gilgit and Armed Forces Institute of Mental Health (AFIMH), Rawalpindi Pakistan, from Sep 2023 to Jan 2024.
Methodology: A total of 247 individuals (147 adult Schizophrenia patients and 100 controls) were included. The Montreal Cognitive Assessment test (MoCA) Urdu 7.1 version was used to assess the cognitive deficits in both patient (cases) and control groups. Various clinical factors were also assessed for association with cognitive deficits among cases.
Results: Among the total 247 study participants, the mean age was 31.97±7.63 years. One hundred and seventy-eight (27.9%) individuals were male and 69(27.9%) were females. Average MoCA score of the control group was 27.56±3.30 and average MoCA score for the cases was 20.63±3.89, with highly statistically significant difference (p-value <0.001) between cases and controls. There was signification association of cognitive deficits with earlier age of onset of illness, smoking, current use of depot antipsychotic injections, treatment with combined and atypical antipsychotics and higher anticholinergic burden score, greater number of previous psychiatric admissions, job status (unemployment) and a family history of psychiatric Illness.
Conclusion: Cognitive impairment is more frequently seen in Schizophrenia patients as compared to controls, with several cognitive domains significantly impacted including attention, concentration, executive functions and visuo-spatial abilities.

Keywords: Cognitive Impairment, Montreal Cognitive Assessment Test (MoCA), Schizophrenia.

How to Cite This Article: *Shabbir A, Ali S, Sharif AMB, Ijaz S, Khan MA, Nohman M. Deficits in Adult Schizophrenia and its Association with Clinical Factors. Pak Armed Forces Med J 2025; 75(4): 717-721. DOI: https://doi.org/10.51253/pafmj.v75i4.11621*

INTRODUCTION

Schizophrenia is a complex mental disorder which affects roughly 20 million people across the globe.[1] Worldwide, Schizophrenia ranks third among leading causes of death in those aged 15 to 44 and has an estimated prevalence of 1-2% in Pakistan.[2]

Various studies demonstrate that cognitive impairments are frequent in Schizophrenia. Cognitive deficits often manifest as challenges in memory, attention, and problem-solving skills.[3,4] Generally prevalence rates of around 80% are quoted, i.e., one standard deviation below population average.[5-7] Although the cognitive areas thought to be most impacted include working memory, verbal fluency, verbal learning and memory, and executive functioning, research has shown that verbal memory and executive functions are affected the most.[7]

Researchers have also looked into possible global correlates of cognitive impairment. Some of the characteristics that have been linked to more severe cognitive impairment include being male, having low educational attainment, advancing age, starting the condition earlier in life, having metabolic risk factors, using antipsychotics at a higher dose, using anticholinergic medications, and smoking.[6,8]

There is a dearth of information pertaining to Asian populations, despite the fact that cognitive dysfunction in Schizophrenia has been extensively researched in Western nations. Our study is justified by the information vacuum that has been formed by the poor data related to cognitive abnormalities in Schizophrenia patients in this region, especially Pakistan. The goals of the study were to determine the prevalence of cognitive impairment in Schizophrenia patients, the extent/severity to which it was present in different areas of cognitive functioning, compare the presence of cognitive impairment with non-psychiatric controls and to look at different clinical and socio-demographic variables that may have contributed to this impairment.

METHODOLOGY

This Comparative cross-sectional study was conducted at Psychiatry Department, Combined

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Received: 09 Feb 2024; revision received: 08 Apr 2024; accepted: 15 Apr 2024

Military Hospital (CMH), Gilgit and Armed Forces Institute of Mental Health (AFIMH), Rawalpindi Pakistan, from September 2023 to January 2024. Approval from taken from Ethical Review Boards of CMH Gilgit and AFIMH Rawalpindi respectively.

Inclusion Criteria: Patients of either gender, aged 18-50 years, who met the Diagnostic and Statistical Manual of Mental Disorders (DSM), 5th edition criteria for Schizophrenia were included as cases, while age and gender matched individuals without a personal or family history of psychiatric, neurological or autoimmune disorders were included.

Exclusion Criteria: Patients having acute psychotic symptoms, those with a recent history of Electroconvulsive therapy (ECT) or head injury within the last 3 months, recent intracranial infection, delirium or stroke, epilepsy, intellectual disability, neurodegenerative diseases like dementia, comorbid substance abuse, depression or mood related illness and autoimmune disorders were excluded.

The sample size was calculated WHO sample size calculator, assuming 80% power of test, expected prevalence of cognitive impairment among patients with schizophrenia (p=89.3%), margin of error of 5% (d) and confidence level of 95% (Z).[9]

A total of 247 individuals were recruited in the study through consecutive sampling after obtaining informed consent (147 adult Schizophrenia patients and 100 age and gender matched non- psychiatric controls). The Montreal Cognitive Assessment test (MoCA) Urdu 7.1 version was applied to both cases and controls. Permission to use the MoCA was obtained from copyright organization MoCA Cognition®. A detailed clinical history was also taken from each patient regarding the possible clinical and socio-demographic factors which could be associated with cognitive impairment. The clinico-demographic factors included: age, gender, marital status, duration of illness, age of onset of illness, employment status, current medications, anticholinergic burden score (ACB), previous psychiatric admissions, previous Electroconvulsive therapy (ECT) sessions (not within last 3 months) and head injury (before illness onset), current smoking status, family history of psychiatric illness, and present use of depot antipsychotic injections. Association of cognitive deficits with the clinical factors mentioned above was assessed.

Montreal Cognitive Assessment test (MoCA) is a highly sensitive screening test for early detection of mild cognitive impairment MCI.[10,11] It has a sensitivity of more than 90% for detecting MCI as compared to 25.9% for the Mini Mental State Examination MMSE.[10] It assesses the following seven cognitive domains: attention and concentration (6 points), executive/ visuo-constructional functions (5 points), language (3 points), naming (3 points), abstraction (2 points), recall (5 points) and orientation (6 points). Montreal Cognitive Assessment test (MoCA) has a maximum score of 30 points. A final total score of 26 and above is considered normal, scores for mild cognitive impairment range from 18-25, for moderate cognitive impairment: 10-17 and scores under 10 points show severe cognitive impairment.[10]

Anticholinergic burden score (ACB) for the medication being used by each patient in Schizophrenia group was calculated using the ACB calculator by Dr. Rebecca King and Steve Rabino (acbcalc.com). A score of 3+ is associated with an increased cognitive impairment and mortality.[12]

Data was analyzed using Statistical Package for the Social Sciences (SPSS) version 23. Mean±SD was calculated for continuous variables. Frequency and percentages were calculated for categorical variables. The Chi square test/Fisher exact test was used to determine presence or absence of statistically significant association of cognitive deficits with clinical factors and independent sample t test was used for the comparison of MoCA Scores, ACB score among the study groups, a p-value ≤0.05 was considered significant.

RESULTS

A total of two hundred and forty-seven (n=247) individuals were included in this study, hundred were normal individuals (controls) and one hundred and forty-seven were Schizophrenia patients (cases). Mean age of the patient group was 31.97±7.63 years. 178(27.9%) patients were male and 69(27.9%) were females. The details of demographic characteristics of both groups (cases and controls) are shown in Table-I. There was no statistically significant difference among the cases and control groups with respect to gender (p=0.240) and age (p=0.580) while marital status (p=0.026), education (p=0.019) and smoking status (p=0.007) showed significant difference.

Average MoCA score of control group was 27.56±3.30 and in cases, MoCA average score was 20.63±3.89 with a highly statistically significant difference seen between the cases and controls (p-value <0.001), as shown in Table-II. Seventy-seven (52.4%) cases had mild cognitive impairment and

52(35.4%) had moderate cognitive impairment according to MoCA scoring. Majority of cases were on atypical (second generation) antipsychotic treatment 84(57.1%) and combined antipsychotics 47(32.0%). Sixteen (10.9%) cases were using typical (first generation) antipsychotics, and 32 patients were using Depot antipsychotic injections, out of which 20(13.6%) patients were on Fluphenazine depot injection, 8(5.4%) were using injection Zuclopenthixol depot and 4(2.7%) were on Flupenthixol depot injection. Seventy-five (51.02%) cases were smokers. Furthermore, 61(41.5%) cases had a family history of psychiatric illness. On the other hand, only 11 controls (0.11%) had a family history of psychiatric illness. Nine (6.1%) cases had a history of head injury prior to Schizophrenia onset and 50 cases (34.01%) had a previous history of Electroconvulsive therapy (not within last 3 months). Most cases (63.9%) had illness onset between the ages of 21-30 years and 119 cases (80.9%) had a history of past psychiatric admissions. The average ACB Score of cases was 5.95±1.86.

Table-I: Association of Demographic Characteristics across Cases and Controls (n=247)

Variables	Control (n=100)	Cases (n=147)	*p*-value
Age in Years	32.25±7.66	31.76±0.62	0.580
Gender			
Male	68(68.0%)	110(74.8%)	0.240
Female	32(32.0%)	37(25.2%)	
Marital status			
Single	38(38.0%)	82(56.2%)	0.026
Married	56(56.0%)	54(37.0%)	
Divorced	5(5%)	8(5.4%)	
Widower	1(1.0%)	3(2.0%)	
Education			
Below Matric	19(19.0%)	57(38.5%)	0.019
Matric	47(47.0%)	57(38.5%)	
Intermediate	21(21.0%)	20(13.6%)	
Bachelors	12(12.0)	11(7.5%)	
Masters	1(1.0%)	2(1.4%)	
Smoking Status			
Yes	29(29.0%)	75(51.0%)	0.007
No	71(71.0%)	72(49.0%)	

During statistical analysis, no statistically significant association was seen between cognitive impairment and gender (p=0.585), age (p=0.639), education (p=0.395), head injury before illness onset (p=0.106) and previous history of ECTs (p=0.120). A significant association of cognitive deficits was found with smoking (p<0.032), current use of depot injections (p<0.001), family history of psychiatric illness (p<0.001), number of previous psychiatric admissions (p<0.001) and job status-unemployment (p<0.001), treatment history (p<0.001), ACB score (p<0.001), age of onset illness (p=0.012) and duration of illness (p=0.014) as shown in Table-III.

Table-II: Comparison of MoCA Scores Between Cases and Control (n=247)

Variable	Control (n=100)	Cases (n=147)	*p*-value
MoCA Scores	27.56±3.30	20.63±3.89	<0.001
Cognitive Impairment Among Cases (n=147)			
Normal MoCA scores			18(12.2%)
Mild Cognitive Impairment			77(52.4%)
Moderate Cognitive Impairment			52(35.4%)

MoCA: Montreal Cognitive Assessment test

Table-III: Association of Cognitive Deficits with Various Clinical Factors of Schizophrenia Patients (n=147)

Factors	Degree of Cognitive impairment			*p*-value
	No Cognitive Impairment (n=18)	Mild (n=77)	Moderate (n=52)	
Smoking Status				
Yes	10(56.6%)	46(59.7%)	19(36.5%)	0.032
No	8(44.4%)	31(40.3%)	33(63.5%)	
Current use of Depot Injections				
Nil	18(100.0%)	71(92.20%)	26(50.0%)	<0.001
Yes- Fluphenazine	0(0%)	4(5.19%)	19(36.53%)	
Yes- Zuclopenthixol	0(0%)	2(2.59%)	7(13.46%)	
Family History of Psychiatric Illness				
Present	12(66.7%)	56(72.7%)	18(34.6%)	<0.001
Absent	6(33.3%)	21(27.3%)	34(65.4%)	
Number of Previous Psychiatric Admissions				
Nil	10(55.6%)	17(22.1%)	1(1.9%)	<0.001
1–2	8(44.4%)	52(67.5%)	36(69.2%)	
3–5	0(0%)	8(10.4%)	15(28.8%)	
Job Status				
Unemployed	9(50.0%)	44(57.1%)	49(92.2%)	<0.001
Employed	9(50.0%)	33(42.9%)	3(5.8%)	
ACB Score	4.11±4.11	5.22±1.55	7.69±1.87	<0.001
Treatment History				
Atypical antipsychotic	15(83.3%)	58(75.3%)	11(21.2%)	<0.001
Typical antipsychotic	3(16.7%)	8(10.4%)	5(9.6%)	
Combination of Atypical/Typical antipsychotics	0(0%)	11(14.3%)	36(69.2%)	
Age of illness				
≤20 Years	4(22.2%)	13(16.9%)	21(40.4%)	0.012
21–30 Years	10(55.6%)	55(71.4%)	29(55.8%)	
>30 Years	4(22.2%)	9(11.7%)	1(3.8%)	
Duration of illness				
≤ before 2015	5(27.8%)	23(29.9%)	28(53.8%)	0.014
> after 2015	13(72.2%)	54(70.1%)	24(46.2%)	

ACB: Anti Cholinergic Burden

DISCUSSION

This study found cognitive impairment among 87.8% of the patients in our sample, consistent with results of previous studies which have reported rates between 80% and 90%.[5,6] A previous study conducted on Thai patients, using the Montreal Cognitive

Assessment Tool, found that 81.3% of the participants exhibited a notable degree of cognitive impairment (MoCA-T).[13] However, the sample size of the aforementioned study was somewhat small (75 participants) and only patients from OPDs were recruited. This Thai study also found that patients on combined antipsychotics showed greater cognitive impairment, similar to our results. Another study in Bulgaria followed 105 Schizophrenia patients over the course of 4 years and found deficits in working memory and attention, especially in those patients who were resistant to treatment. However, they found no statistically significant difference between genders with regards to cognitive deficits.[14] Patients with persistent Schizophrenia and those experiencing their first episode had lower scores than the typical control group, according to another study.[15] Thus, our study's results provide more evidence that cognitive impairment is a fundamental aspect of Schizophrenia.

Mean scores below the lower limit of normative values were observed in all seven cognitive domains examined in our data, including attention, memory, fluency, language, and visuo-spatial skills. The scientific community is divided on whether all cognitive areas are equally impaired or if certain domains are affected more severely in schizophrenia. In a USA study, 183 Schizophrenia patients underwent the detailed MATRICS battery and processing speed was identified to be the most affected cognitive domain.[16] On the other hand, an expert review paper states that it is better to look at cognitive deficits in Schizophrenia patients as a generalized entity, rather than specific domain deficits.[17] The majority of our study participants had difficulties in the memory domain. There were some changes in the percentage of patients impacted across the domains, but the Poisson log-linear analysis found no statistically significant differences. Accordingly, this lends credence to the idea that schizophrenia-related cognitive impairment is likely to be systemic rather than domain-specific.[17]

One point of note is that we did not find a significant association between levels of education and degree of cognitive impairment in our study. This finding contrasts with previous studies which note that patients with lower levels of education display more severe cognitive deficits.[6,7,9] We also found no association of age or gender with cognitive deficits. Regarding job status, we found that majority patients in our sample were unemployed and cognitive deficits were higher in unemployed patients. It is also important to note that even those patients in our sample who were employed, were performing low intensity, non-technical jobs like manual labor, shop keeping, tending to their fields etc. This may reflect the substantial degree of functional impairment caused by Schizophrenia and the inability to perform technical work may the result of cognitive impairment. Moreover, cognitive deficits were also found to be associated with other factors: greater number of previous psychiatric admissions, smoking, current use of depot antipsychotics, use of combined and atypical antipsychotics, family history of psychiatric illness, onset of illness before 30 years of age and higher anticholinergic burden score which is similar to results of previous studies.[18] The current medication trends for psychosis patients in Pakistani psychiatric practice often utilize combinations of antipsychotics to supposedly improve clinical response, which is against the poly pharmacy recommendations by Maudsley Prescribing Guidelines, 14th edition and European Psychiatric Association guidance.[19] This contributes to higher anti-cholinergic burden, which is in turn associated with cognitive deficits. Lifestyle modifications such as smoking cessation also need to be encouraged in Schizophrenia patients due to the association of chronic smoking with cognitive dysfunction,[20] as was demonstrated in our sample as well. Clinicians can also focus on emerging clinical treatments such as repetitive trans-cranial magnetic stimulation (rTMS) which show potential to ameliorate cognitive symptoms.[21]

The importance of identifying cognitive impairment early on in the treatment of schizophrenia is growing in light of its high prevalence and the profound effects it has on patients' outcomes. Routine evaluations in the majority of Pakistani psychiatric facilities do not give patients' cognitive functions the consideration they deserve at this time. This lack of enthusiasm may be due in large part to the therapeutic nihilism that surrounds this topic.

To lessen the blow, cognitive rehabilitation programs should be rolling as soon as possible and Pakistani psychiatrists should be sensitized to the need of encouraging lifestyle changes among Schizophrenia patients and adjusting medication regimes to minimize antipsychotic poly pharmacy and anticholinergic burden.

LIMITATION OF STUDY

We found a number of points where this study fell short. As an observational, case control study, while associations were drawn with various demographic and clinical factors, causation cannot be inferred. Due to limited sample size, is possible that the sample did not adequately represent the population. Also, rather than providing a comprehensive picture of a patients' medication history, only current medication data was presented in our study.

CONCLUSION

Cognitive impairment is more frequently seen in Schizophrenia patients as compared to controls, with several cognitive domains significantly impacted including attention, concentration, executive functions and visuo-spatial abilities.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

AS & SA: Data acquisition, data analysis, critical review, approval of the final version to be published.

AMBS & SI: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MAK & MN: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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