Psychometric Evaluation of Paediatric Patients with Central Nervous System Demyelination

By

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ABSTRACT:

Background: *Psychosocial evaluation in patients with demyelinating diseases has been predominantly examined in adults. Only a few studies were conducted on children with demyelinating diseases to study neuropsychiatric impairment.*

Aim: *to assess the neuropsychiatric comorbidities and behavioural problems in children with central nervous system (CNS) demyelinating diseases, as well as to determine the effect of these comorbidities on the quality of life (QoL).*

***Methods**: this is a case-control study that was done during the period from December 2022 till june 2023, the patients were randomly selected from child neurology clinic, faculty of medicine, Ain Shams University Hospital. This study included twenty-eight children diagnosed with CNS demyelination as well as 28 healthy children with matched age, sex, and social class were enrolled in this study as a control. The neuropsychiatric evaluation was performed by clinical examination and three psychometric scales : (1) Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS) (2) Child Behaviour Checklist (CBCL) (3) Kid-Screen 27. The assessments were conducted between 1 and 18 months (median 8 months) after the acute illness.*

Results: *There were clinically significant anxiety in 64.3%, and depressive symptoms in 93%. Impaired attention was detected in 17.9% of the patients. Patients with demyelination experienced more behavioural problems than control, the CBCL internalizing and externalizing symptoms scores were in the clinical range for 85.7%, 42.9% of the participants, Patients with demyelination had lower scores for QoL than control (P= 0.001). Psychological comorbidities such as depression, anxiety, attention problems, and oppositional defiant were the main determinants for low QoL.*

Conclusion: *neuropsychiatric symptoms and behavioural problems are not uncommon among paediatric patients with CNS demyelinating disorders. Our data showed that demyelination diseases might have mental health sequelae long after the resolution of the acute attack which has a deleterious effect on quality of life.*

Keywords: *Demyelinating, children, psychiatric*

Introduction:

Central Nervous System (CNS) demyelination is a condition characterized by the damage or destruction of the protective covering (myelin) of nerve fibers in the brain and spinal cord. While it can occur in individuals of all ages, it is particularly significant in children **(Canavese et al., 2023; Chitnis, 2019).**

CNS demyelination in children encompasses a spectrum of disorders, including multiple sclerosis (MS) and acute disseminated encephalomyelitis (ADEM). While these conditions are relatively rare in paediatric populations compared to adults, they still represent a significant burden **(Troxell & Christy, 2019).**

Furthermore, chronic fatigue is a common symptom in children with CNS demyelination and can significantly impact their daily activities and quality of life. Also, children may experience difficulties with memory, attention, concentration, and problem-solving. They may also exhibit mood swings, irritability, or changes in behaviour. **(Dale et al., 2009; Hintzen et al., 2016)**

Since CNS demyelination can impact various aspects of a child's cognitive, behavioural, and emotional functioning, conducting comprehensive psychometric assessments is essential to understand the impact of the disease and guide appropriate interventions **(Coutinho Costa et al., 2023; Tan et al., 2021).**

Given the rising incidence of mental health disorders in children and teens **(Sadler et al., 2018)** it's critical to comprehend how diseases like demyelinating illnesses affect these conditions. All paediatric demyelinating disease patients must deal with the difficulties of adjusting to a severe illness at a time when their psychological, emotional, and social development is at its most vulnerable. Paediatric patients must cope with the disorder's unpredictable nature, uncertainty about the future, relative isolation, and feeling of being "different" from peers in addition to adjusting to its wide range of probable symptoms **(Alroughani & Boyko, 2018)**.

One of the key purposes of psychometric evaluation in paediatric patients with CNS demyelination is to establish a baseline assessment of their cognitive functioning. The baseline assessment of cognitive functioning allows for tracking changes over time and monitoring the impact of the disease on various cognitive domains. It helps in identifying specific areas of impairment, guiding intervention planning, and evaluating treatment outcomes **(Alroughani & Boyko, 2018; Hintzen et al., 2016)**. Therefore, in the current research, the primary aim is to assess the psychiatric disorders in children with CNS demyelinating diseases, while the secondary aim is to assess the quality of life of these patients.

Study procedure :

Participants:

This is a case-control study that was conducted over 6 months. The study included 28 children with CNS demyelination who were on regular follow-up in the Pediatric Neurology Clinic, Faculty of Medicine, Ain Shams University, and 28 control participants with matched age, sex, and social class. The assessments were conducted between 1 and 18 months after the acute attack of demyelination.

Ethical consideration:

- Approval by the Ethics Committee of the paediatrics department at the faculty of medicine at Ain Shams University under the registration number was obtained before the study
- Patients were enrolled in the study after getting informed oral and written consent from their parents.
- Patient data confidentiality was preserved during all study procedures.
- The patient and parents have the right to withdraw at any time.
- There was no conflict of interest regarding the study or publication .
- There is no financial support or sponsorship.

Sample size: The sample size was calculated using PASS 11 program for sample size calculation, setting Power at 80% and α-error at 0.05, and according to ***Weisbrot et al., (2010)*** who reported a prevalence of psychiatric disorders in paediatric patients with demyelination disorders to be 48%. A sample size of 28 patients per group produces a two-sided 95% confidence interval with a width equal to 0.35 when the sample proportion is 0.480.

Inclusion criteria:

1. Age: 6-18 years old.
2. Children diagnosed as CNS demyelinating disorders.

Exclusion criteria: patients with

1. Any systemic disorder.
2. Inborn errors of metabolism.

3. Behavioral or developmental disease prior to CNS demyelination.

Study procedure:

All participants were subjected to

(1) **full history taking with special emphasis on** the type and course of demyelination disorder, times of relapse if present and the treatment received.

(2) A **complete neurological examination** was done for all participants.

(3)All the studied cases were subjected to the following:

- **The updated version of the Arabic socio-economic status (SES) scale originally developed by Fahmy and El-Sherbini (1983)** was used. It covered seven areas, including family, economics, education and culture, household goods, home hygiene, and health care. The scale's scoring is categorised as high, middle, low, or extremely low socioeconomic status based on the quartile of the calculated score **(El-Gilany, 2012).**

- **Kiddie Schedule for Affective Disorders and Schizophrenia Present and Lifetime version (KSADS-PL) Arabic version.** The validated test includes a semi-structured interview to assess symptoms suggestive of mood, anxiety, psychotic, and disruptive behaviour disorders in children between 6 and18 years of age. It aims at early diagnosis of several mental disorders including, depression, mania, panic, separation anxiety, phobia, overanxiety, obsessive compulsive disorder, ADHD, oppositional and conduct disorders ***(Kaufman et al., 2004).***The Arabic version was validated by **Moussa et al., 2011**
- **Arabic version of Child Behaviour Checklist** (CBCL/6–18) is designed to assess behavioural, social and emotional problems in children aged 6–18 years.

  It includes 113 parent- reported measures for several sub-scales, including Withdrawn Somatic Complaints, Anxious/Depressed, Rule-Breaking Behaviour, Social Problems, Thought Problems, Attention Problems, and Aggressive Behaviour. The severity of the behaviour is determined using a 3-point Likert scale values of 0 = no, 1 = occasionally, and 2 = very often. Three summary scales can be obtained from CBCL, the total scores as well as the scores for internalizing and externalizing difficulties. The Internalising domain is a comprehensive indicator for emotional disorders including Emotionally Reactive Behaviour, Anxious/Depressed Behaviour, Somatic Complaints, and Withdrawn Behaviour. The Externalizing domain is an overall indicator of behavioural problems and includes aggressive behaviour and attention problems. The CBCL scales have a t-score mean of 50 and a standard deviation of 10. A *t*-score $\leq$ 59 means absence of clinical symptoms, a *t*-score between 60 and 64 indicates a risk for problem behaviours, and a *t*-score $\geq$ 65 illustrates the presence of clinical symptoms ***(Achenbach et al., 2001).*** The Arabic validation version by **Selim &Ismail (2009).**

- **The KIDSCREEN 27:** The KIDSCREEN-27 is a measure of child and adolescent QoL. The KIDSCREEN-27 measures five dimensions: 1) physical well-being, 2) psychological well-being, 3) autonomy and parent relation, 4) peers and social support, and 5) school environments ***(*Ravens-Sieberer *et al., 2006).***

Statistical Analyses of Data:

The Data entry and statistical analyses were performed using SPSS (Statistical Package of Social Sciences) version 26 (SPSS Inc., Chicago, IL, USA) (Dean, 2006). Continuous normally distributed data was expressed in mean and standard deviation. The quantitative data was examined by the Kolmogorov-Smirnov test for normality of data. Kruscal Wallis test was used for continuous not normally distributed data. Categorical data were described as numbers and percentages and were analyzed using the Chi-square test. Statistical significance was considered when the probability (P) value was less than or equal to 0.05.

Results:
Our results will be demonstrated in the following tables and figures:

Table (1): Socio-demographic and clinical data of all participants:

Socio-demographic data	Patients group (n=28)	Control group (n=28)	p-value
Age (years)			
Mean± SD	9.84±2.39	8.36±2.13	0.277
Range	6-14	5-15	
Sex			
Male	10 (35.7%)	13 (46.4%)	0.415
Female	18 (64.3%)	15 (53.6%)	
Socio economic level*			
Low Level	6 (21.4%)	7 (25.0%)	
Middle Level	19 (67.9%)	15 (53.6%)	0.461
High Level	3 (10.7%)	6 (21.4%)	

This table shows insignificant difference between cases &control regarding demographic data
*Socioeconomic level detected according to SES scale (The updated version of the Arabic Socio-economic status)

Table (2): Symptoms and diagnoses of included patients:

Symptoms at presentation	N (%)
disturbed conscious level	7 (25.0%)
Inability to walk	17 (60.7%)
Vision affection	17 (60.7%)
Autonomic affection	9 (32.1%)
Diagnosis	
Acute disseminated encephalomyelitis	6 (21.4%)
Cerebellar demyelination	1 (3.6%)
Clinically isolated Demyelination	5 (17.9%)
Transverse myelitis	4 (14.3%)
Neuromyelitis Optica	5 (17.9%)
Optic neuritis	7 (25.0%)

This table shows that inability to walk and vision affection were the most common symptom
And the most diagnosis was optic neuritis followed by Acute disseminated encephalomyelitis.

Table (3): Comparison between patients' group and control group according to KSADS scale

KSADS	Patients group (n=28)	Control group (n=28)	p-value
Depression	26 (92.9%)	1 (3.6%)	0.000
Mania	5 (17.9%)	0 (0.0%)	0.012
Panic	10 (35.7%)	1 (3.6%)	0.004
Separation	14 (50.0%)	1 (3.6%)	0.000
Phobic	7 (25.0%)	0 (0.0%)	0.000
Overanxious	18 (64.3%)	2 (7.1%)	0.000
Obsessive Compulsive disorder	4 (14.3%)	0 (0.0%)	0.018
ADHD	5 (17.9%)	0 (0.0%)	0.003
Oppositional disorders	12 (42.9%)	0 (0.0%)	0.000
Conduct disorders	1 (3.6%)	2 (7.1%)	0.724

This table shows that there was statistically significant difference between patients and controls group regarding depression separation, phobic, overanxious, and oppositional ($p<0.01$). Mania ($p=0.012$); panic ($p=0.004$); obsessive compulsive disorders ($p=0.018$) and ADHD ($p=0.003$).

Table (4): Number and percent of Children at or Above the Clinical Range for the CBCL Scales ($t \geq 65$)

Competence Scales	Patients (n=28)	Control (n=28)	p-value
Broadband scales			
Total score	25 (89.3%)	0	0.000
Internalizing level	24 (85.7%)	0	0.000
Externalizing level	12 (42.9%)	0	0.000
Syndrome scales			
Anxious/Depressed	26 (92.9%)	0	0.000
Withdrawn/Depressed	14 (50.0%)	0	0.000
Somatic Complaints	17 (60.7%)	0	0.000
Social Problems	17 (60.7%)	0	0.000
Thought Problems	7 (25.0%)	0	0.001
Attention Problems	9 (32.1%)	0	0.000
Rule–breaking Behaviour	2 (7.1%)	0	0.064
Aggressive Behaviour level	6 (21.4%)	0	0.000
Competence scale			
School level	8 (28.6%)	0	0.002

This table shows that Independent samples t-tests revealed significantly more behavioural problems (indicated by higher CBCL scores) in the patient group compared to the control group (Total scores P, <0.01,

Table (5): Comparison between Patients group and control group according to Kid Screen 27

Kid Screen 27	Patients group (n=28)	Control group (n=28)	p-value
Physical well-being	12.9 (9.4-13.5)	13.5 (10.4-13.5)	0.098
Psychological well-being	14.1 (10.8-17.6)	19.3 (15.3-21.2)	0.001
Parent relations & Autonomy	23.7 (22.8-24.6)	30.0 (23.7-30.0)	0.001
Social Support & pears	6.9 (5.4-8.3)	8.8 (7.0-8.8)	0.001
School Environment	4.9 (4.0-6.4)	9.0 (7.0-9.0)	0.001
Total score of Kid Screen 27	52 (54-68)	74 (67-82)	0.001

Data presented in "Median (IQR: Interquartile range)"
This table shows that there were statistically significant differences between patients and control groups regarding the median of psychological well-being (p<0.01); parent relations & autonomy (p<0.01); social support and peers (p<0.01), and school environment (p<0.01) as well as total score. However, there was no significant difference in physical well-being (table 5).

Table (6): Correlation between Kid Screen 27 and KSADS in patients' group, using Spearman's rank correlation coefficient.

KSADS	Kid Screen 27									
	Physical wellbeing		Psychological wellbeing		Parent relations & Autonomy		Social Support & pears		School Environment	
	R	P	R	P	R	p	R	P	r	p
Depression	-0.199	0.141	-0.362	**0.006**	-0.427	**0.001**	-0.479	**0.000**	-0.640	**0.000**
Mania	-0.325	**0.015**	-0.362	**0.006**	-0.192	0.156	-0.234	0.082	-0.213	0.115
Panic	-0.035	0.798	-0.312	**0.019**	-0.252	0.061	-0.205	0.129	-0.285	**0.033**
Separation	-0.271	**0.043**	-0.267	**0.047**	-0.173	0.202	-0.364	**0.006**	-0.466	**0.000**
Phobic	-0.193	0.153	-0.455	**0.000**	-0.424	**0.001**	-0.334	**0.012**	-0.560	**0.000**
Overanxious	-0.166	0.222	-0.381	**0.004**	-0.295	**0.027**	-0.454	**0.000**	-0.591	**0.000**
Obsessive Compulsive disorder	-0.136	0.317	-0.188	0.166	-0.178	0.190	-0.217	0.108	-0.263	**0.050**
ADHD	-0.420	**0.001**	-0.378	**0.004**	-0.197	0.146	-0.401	**0.002**	-0.600	**0.000**
Oppositional disorders	-0.262	0.051	-0.356	**0.007**	-0.403	**0.002**	-0.340	**0.010**	-0.503	**0.000**
Conduct disorders	0.067	0.624	0.161	0.235	0.029	0.830	-0.060	0.660	0.008	0.954

This table shows that Psychological comorbidities had a negative effect on the quality of life especially depression, separation, panic, anxiety, ADHD, and oppositional (P= <0.01, <0.01, 0.033, <0.01, <0.01, <0.01 respectively).

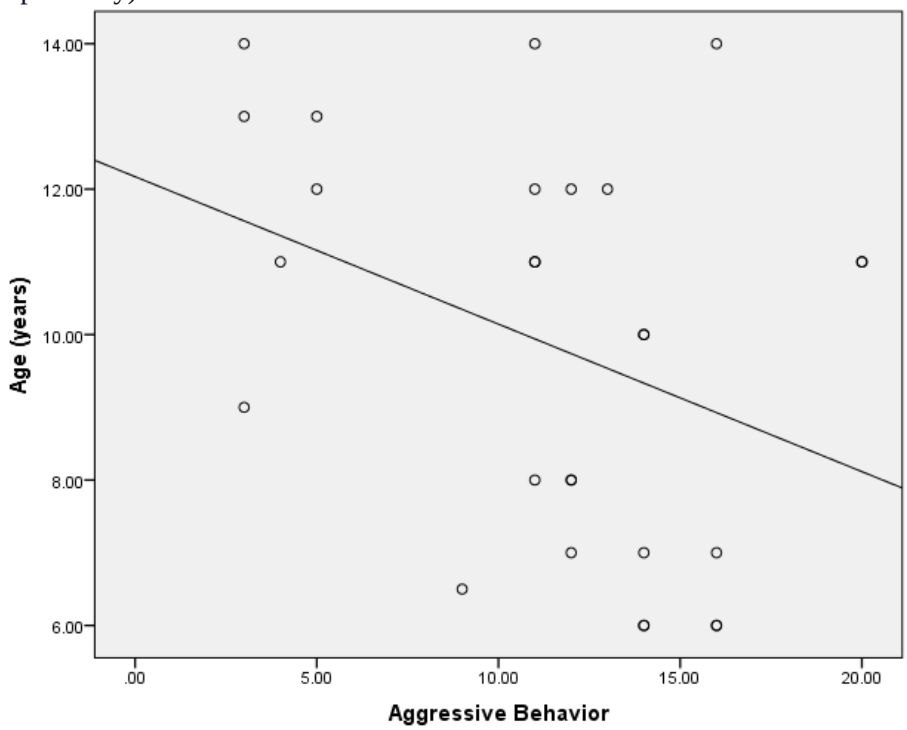

Figure (1) Correlation between age aggressive behaviour

This figure shows that There was a statistically significant negative correlation between CBCL aggressive behaviour and age (p=0.030);

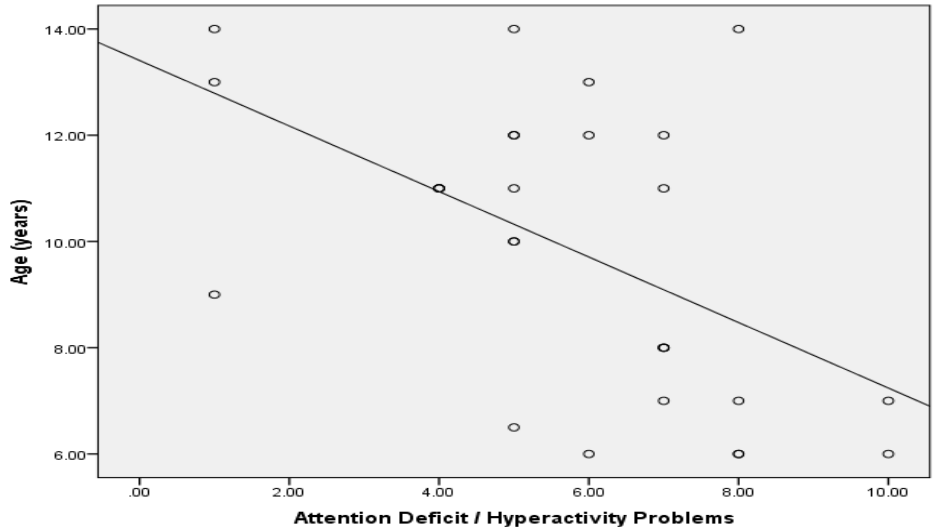

Figure (2) Correlation between age and attention deficit/ hyperactivity.

univariate logistic regression failed to prove an association between the presence of depression or anxiety and the studied factors including age, sex, living area, school performance, socio-economic level, vision affection, inability to walk, and autonomic affection.

Discussion:

In This case-control study found that the rates of depressive and anxiety symptoms as well as behavioural problems were higher in children with CNS demyelination than population norms.

CNS demyelination diseases have been linked to a higher chance of psychiatric disorders in paediatric patients **(Konuskan & Anlar, 2019)**. CNS demyelination diseases and psychiatric disorders share underlying pathophysiological mechanisms that involve inflammation, immune dysregulation, and neurotransmitter imbalances. The disruption of myelin in the CNS can lead to alterations in neural circuitry and communication, potentially affecting mood regulation, cognition, and behaviour **(Chitnis, 2019)**.

In the current research, we found that depression was the most frequent psychiatric comorbidity in patient with CNS demyelination (93%) followed by anxiety (64%) with significant differences between patients and control groups.

A previous multicenter study conducted on childhood and juvenile MS, found that depression was te most common psychiatric disorder among their cohort **(Amato et al., 2010)**.

Goretti et al. reported that 15% of their children with MS were given a formal diagnosis of depression using KSADS-PL (**Goretti et al., 2010)**

Our results showed higher percentage of psychiatric comorbidities in comparison to earlier studies that reported around 50% of children with CNS demyelination have suffered from depression, anxiety, or coping disorders **(Banwell &Anderson, 2005; MacAllister et al., 2005; Amato et al., 2008).**

These psychiatric complications could be explained by several factors. Firstly, coping with the physical limitations, and potential disability can lead to increased stress, anxiety, and depression. The psychosocial burden of living with a chronic illness and uncertainty about disease progression may contribute to the development of psychiatric symptoms **(Chesson et al., 2004; Grey et al., 1991; Kager & Holden, 1992).**

We found a significant reduced school level competence Scales using CBCL, among patients with CNS demyelination.

Amato et al. indicated that CNS demyelinating disorders had a detrimental impact on school and daily activities in 56% of their cohort and they found 8% of the individuals had a relatively low IQ (<70) **(Amato et al., 2008)**. According to one study, cognitive impairment was identified in 80% of pediatric patients with MS who met the criteria for a psychiatric condition, as opposed to 55% of those who did not. In addition, as compared to other psychiatric diagnoses, anxiety or mood disorders had the extreme likelihood of associated cognitive impairment **(Weisbrot et al., 2014).**

Beatty et al. found that psychological issues were reported by 20%–40% of patients with ADEM, and that 22.7% of patients had impairments on three or more neurocognitive assessments **(Beatty et al., 2016).**

However, **Till et al.** found no differences in the cognitive, academic, or behavioural results between the patients with CNS demyelinating disorders and the controls **(Till et al., 2016)**.

As regards QoL assessment in this study using Kid screen 27, there were statistically significant decrease of QoL scales in patients' group in comparison to control groups.

Similarly, demyelinating illnesses have been linked to a lower quality of life, impacting young people's emotional, social, behavioural, and academic performance especially in multiple sclerosis **(Duncan et al., 2020).**

Lanzillo et al. reported that QoL was negatively affected in MS, and it inversely related to the disability scores **(lanzillo et al., 2016).**

We found a negative correlation between age and some behavioural problems as aggression, and attention problems. This is supported by **Jacobs et al.** highlighted that children with more serious behavioural and emotional issues have been diagnosed with ADEM before the age of five **(Jacob et al., 2004).**

Furthermore, **Beatty et al.** noted that a younger age at which ADEM manifests itself is associated with an increased risk of behavioural disorders and intellectual impairment. **(Beatty et al., 2016).**

The substantial correlation between the age at which demyelination is diagnosed and behavioural changes might be explained by the fact that axonal myelinization and synaptic density have a strong correlation with functional development and white matter develops at the quickest rate in early life (**Deery et al., 2010).** Specifically, between the ages of 3 and 7 years, there was a noticeable increase in synapse density and axonal myelinization **(Tideman & Gustafsson, 2004).**

Conclusion:
The idea that CNS demyelination may have distal neuropsychiatric consequences is supported by the high rates of anxiety, depression, attention issues, and behavioural issues that were observed in this group of children following acute demyelination. These data can be helpful in identifying the kinds of symptoms that may be linked to demyelination and emphasising the clinical significance of investigating the neuropsychiatric consequences of CNS demyelination in more detail.

Recommendation: children with CNS demyelination should early undergo psychiatric evaluation.

Limitation:
It is vital to acknowledge certain limits. The sample size was small to begin with. Second, there were no baseline pre-demyelination neuropsychiatric or neurocognitive examinations available; as a result, the research participants had never been professionally tested and were not known to have neuropsychiatric symptoms or academic, social, or familial challenges

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