Journal of Psychiatry

OPEN ACCESS Freely available online

Research Article

Neuropsychiatric Manifestations of Wilson Disease in Sudan

Hussein Jafar Elhafyan[1*], Abdelgadir Hussein M Osman[2], Yahia Ownalla Younis[3]

[1]Specialist Psychiatry Unit, University of Kassala, Kassala Sudan; [2]Department of Psychiatry, Faculty of Medicine, University of Khartoum, Sudan; [3]Department of Psychiatry, Faculty of Medicine, International University of Africa, Khartoum, Sudan

ABSTRACT

Background: Delineating the neuropsychiatric pattern and features of Wilson disease is essential step to better recognition and management of these presentations. To our knowledge this is the first large study of neuropsychiatric manifestations of Wilson disease in Sudan.

Method: A comprehensive case finding survey was conducted over a six month period, in the Capital of Sudan, covering all secondary and tertiary services that cater for patients with Wilson disease. Patients' assessment was carried out using batteries of functional tests, including, ICD-10 research criteria for major psychiatric categories, Mini Mental State Examination, ADHD scale, school records, parental reports. All neurological findings were conducted and verified by two neurologists.

Results: Fifty cases of Wilson disease, of varying age and stage of illness, were thoroughly examined for neuropsychiatric symptoms and disorders. Most patients 29 (58%) showed psychological disturbance in form of psychiatric illness and significant behavioural disturbance. Mood and emotional disorders observed in 21 (42%) of cases, core symptoms of depressive disorder diagnosed in 19 cases (38%), behavioural and personality disturbances detected in 19 patients (38%), while cognitive impairments were found in 24 (48%) of all cases. Twenty-one cases (42%) presented with neurological abnormalities, predominantly consisting of posturing in 20 (40%), dystonia in 8 (16%), Parkinsonism was found in 10 (20%) patients, dysarthria in 9 (18%), athetosis in 3 (6%) cases and various forms of tremors in 21 (42%). Epilepsy was recorded in 3 cases (6%).

Conclusion: Neuropsychiatric symptoms and disorders are highly prevalent in Wilson disease patients regardless of age, or stage of illness. Even though, patients in our sample had had an average of 6 years follow up duration, non-had shown evidence of liver failure. This shows an early indication of possibly benign trajectory course of the illness in Sudan.

Keywords: Neurological presentation; Neuropsychiatric presentation; Psychiatric presentation; Sudan; Wilson disease

Abbreviations: WD: Wilson Disease; ICD-10: International Classification of Disease; CDDG: Clinical Descriptions and Diagnostic Guidelines; DCR-10: The Diagnostic Criteria for Research accompanying the ICD-10.

INTRODUCTION

Wilson's disease is an autosomal recessive illness that arises due to a defect in the gene ATP7B (on chromosome 13q (long arm)), leading to an impairment in cellular copper transport (packaged in ceruloplasmin into bile), resulting in an excessive accumulation of copper in the liver, brain, cornea, bones and other tissues [1,2]. Over time, this leads to progressive liver damage, eventually culminating in cirrhosis of the liver and, potentially, acute hepatitis. Deposits of the metal in the brain lead to a wide range of neuropsychiatric symptoms and disorders [3-5]. Although the mechanism of copper excretion is defective from birth, most patients present with symptoms between the ages of 5 and 35. A minority do not show symptoms until later in life [6]. The lifetime prevalence of WD is estimated to be 1:30,000 in many countries, although prevalence as high as 1:7000 have been reported [7,8].

Neuropsychiatric syndromes

Neurological or psychiatric symptoms can emerge at any time during the course of the illness; however, the salient pattern of

***Correspondence to:** Abdelgadir Hussein M Osman, Department of Psychiatry, Faculty of Medicine, University of Khartoum, Sudan, Tel: + 249912312117; E-mail: abdelgadir1159@yahoo.com

Received: 01 July 2021; **Accepted:** 23 July 2021; **Published:** 30 July 2021

Citation: Elhafyan HJ etal (2021) Neuropsychiatric Manifestations of Wilson Disease in Sudan. J Psychiatry 24: 477. 24:477. doi: 10.35248/2378-5756.21.24.477

these conditions occurs as a result of subcortical deposition of copper in the basal ganglia, with putamen degeneration or cortical involvement of the frontal lobe [9,10]. In the former, this can result in extrapyramidal symptoms, such as tremors, rigidity, Parkinsonism, chorea, athetosis, ataxia, dysarthria, dysphagia, dystonia, drooling, dysdiadochokinesis, micrographia and coordination problems. Other neurological manifestations include hyperreflexia, tics and unusual stereotyped movement [11-14]. Frontal lobe involvement leads to frontal lobe syndrome, with personality and behavioural abnormalities. Here, patients can present with impulsivity, sexual disinhibition, labile mood [15,16], promiscuity, irritability or apathy, indecisiveness, lack of planning and executive dysfunction. Other psychiatric symptoms and disorders may emerge as a consequence of hepatic encephalopathy, and other organ disorders such as kidney, haemolytic anaemia, endocrine failure, or osteopathy and osteoporosis leading to fractures [17]. By the time patients with WD present with neuropsychiatric symptoms, almost 50% will have developed liver cirrhosis, both of which are preventable with early detection and treatment with chelating agents [18,19]. Neuroimaging advances have shed light on the specific pathology associated with WD. The typical neuroimaging finding of WD is the "face of giant panda" sign, with hyper-intensities in the basal ganglia, tectal plate and the central pons; involvement of the thalamus and brainstem are also characteristic of WD [20,21].

The majority of WD patients present with liver symptoms, however, 30% of patients will present for the first time with psychiatric manifestations. Almost all sufferers will display psychiatric symptoms at some point during the course of the illness [22], and psychiatric presentations often (60%) co-occur with neurological involvement. Little is known of the factors influencing the phenotypic expression of WD (hepatic vs. neurological or psychiatric presentation), although perhaps age of presentation may play a role [23].

The typical psychiatric domains that get affected during the course of WD include affective manifestations, behavioural and personality disturbances, psychosis and cognitive impairments [24].

Cognitive impairment

Cognitive impairment in WD can occur as consequence of brain involvement in the frontal lobe or subcortical structures, or indirectly due to functional insults due to hepatic encephalopathy, endocrine derangement, kidney and blood dyscrasias, and depression. Depending on the underlying cause, the commonest features of cognitive impairments are attention deficit (leading to scholastic problems in school age children), dysgraphia and visuospatial problems; rarely, the cognitive impairments lead to dementia or intellectual decline [25].

Personality changes

The first symptoms to present in children are changes in behaviour, such as over activity, irritability, impulsivity and conduct disorder. Later on, personality changes in adults can arise as a result of neurological involvement of the brain, as in frontal lobe involvement, leading to sexual promiscuity, impulsivity and a lack of ability to make decisions. Behavioural and personality disorders are reported to occur in 46–71% of all WD cases [26,27].

Affective and psychotic disorders

Depression is the commonest reported affective disorder in WD, often associated with behavioural and personality changes. However, at early stage of WD, depression usually manifested with dysthymic, chronic low grade symptoms. Severe forms of depression can occur with suicidal tendencies. [28] Other forms of affected disorders have been well documented, such as mania and bipolar affective disorder, but this yet to be confirmed to have any more prevalence than what can be expected in general population [29].

Schizophrenia like psychosis can occur in WD, often manifest with organic symptoms such as, visual and olfactory hallucinations. Treatment resistant forms of psychosis have been reported, which shows some response following use of chelating agents in combination with atypical antipsychotic medications [30]. Subacute confusion states and delirious disorders occur on advance stages of the illness [31].

The aim of our study therefore, was to indicate the hospital based prevalence of WD in the Capital of Sudan and describe the salient neuropsychiatric presentation of WD. This is the first study in Sudan in its field.

RESEARCH METHODOLOGY

This is a cross-sectional, case finding survey of Wilson disease in Seven Hospitals and Neurological units in the Capital city of Sudan. All are tertiary referral sites, including the main tertiary children's hospitals (3 in Khartoum viz, Al-Shaab Teaching hospital, Ibn Sina Teaching Hospital, Jafar Ibn Aoof Pediatric Hospital and 4 in Omdurman City including, Omdurman Teaching Hospital, Tijani Almaahi Hospital, Friendship teaching Hospital and Sheikh Muhammad Khair Center). These clinics are served by thirteen neurologists and 36 medical doctors in training. They take tertiary referrals for the whole population of the capital of Sudan, approximately five million. All clinics were made aware of the purpose of the research and were able to establish seamless contact with the psychiatrist collating the WD cases. Informal consent was obtained from all patients and parents in case of minors.

Over the six month study period, from December/2011 to May/2012, a total of fifty cases already medically diagnosed with WD were interviewed by a member of the research team. Most of these patients were under follow up (average of 6 years), receiving treatment in form of penicillamine and zinc acetate. All neurological symptoms and signs were verified by neurologists overseeing the specific clinic. A semi-structural psychiatric interview was conducted with individual patients and their relative. Psychiatric symptoms and disorders were then classified according to the ICD-10 diagnostic research criteria for specific psychiatric disorders and syndromes. Incomplete diagnostic diathesis was classified in the domain of personality trait, with a clear mention of the troubling symptoms or traits. Likewise, in the case of cognitive symptoms, a mini-mental state examination was used, together with scholastic records in the case of the school-aged children, to determine cognitive aberrations.

Findings were then classified on four neuropsychiatric domains: neurological, psychiatric disorders, personality traits and cognitive impairment.

Instruments and study tools

A socio-demographic questionnaire was completed for all participants interviewed, and a semi-structured psychiatric interview was conducted with all patients and their relatives in cases where independent corroboration was required and in the case of minors. The diagnostic research criteria for the International Classification of Disease (ICD-10) was adhered to for

classification of disorders and syndromes. The Diagnostic Criteria for Research accompanying the ICD-10 (DCR-10) were utilized for the purpose of classifying categories. These provide specific criteria for diagnosis with associated Clinical Descriptions and Diagnostic Guidelines (CDDG). These guidelines have been used and well tested by researchers and clinicians in over 32 countries [29,30]. The researchers received special training course in the use of the ICD-10 diagnostic criteria. For children behavioural and temperament measure we applied parental report of major changes in four domain, attention impulsivity and hyperactivity sub-domains, confirmed by completing ADHD parental questionnaire Arabic version [30], conduct and difficult behaviour (parental report only),social isolation and withdrawal (parental report) and (hostility and suspiciousness (parental report).

DIAGNOSIS

A diagnosis of Wilson's disease was made on the basis of a low concentration of serum ceruloplasmin and increased urine excretion of copper per 24-hour urine sample, and the presence of a Kayser-Fleischer ring was found in 66% of cases. A family history of Wilson disease was ascertained in 30% of cases. No genetic testing was carried out due to limited resources.

Manifestation of acute hepatic features was usually the diagnostic approach in children seen among the target group of the study. The diagnosis was confirmed by detection of copper in urine collected within 24 hours, i.e., every child who presented to the hospital with hepatic manifestations was investigated for WD. The majority of the urine investigations for copper were carried out in Germany, due to the unavailability of such investigations in Sudan or a low capacity of laboratory technicians to run such specific investigations [31].

Ethics and consent to participate

The study was approved by the Sudanese Medical Specialisation Board, reference number is not applicable. Written permission was obtained from administration departments of the hospitals. Written informed consents were obtained from all participants and their parents in cases of minors. Written information about the study was given beforehand to all participants to explain the purpose of the research. It was explained to all participants that participation was optional, with guaranteed confidentiality.

Statistical analysis

Data was analyzed by an expert statistician using the statistical package for social sciences version 22 (SPSS 22) computer software program. Results were expressed in terms of percentage and frequencies and are shown in Tables 1, 2 and 3.

RESULTS

In a case-finding survey of most neurological clinics in Khartoum, Sudan, over a six-month period, we were able to ascertain diagnosis of fifty cases of WD. These cases were of a heterogeneous nature, both for sex and age, yielding 10 cases per million in a five million population of the capital city of Sudan. Cases were predominated by male sex (31 cases, 62 %,), while 19 cases (38%) were females. The age range of our sample was between 5 and 65. Most cases in our sample were children and young adults under 24 years (32 cases, 64%), while only 7 (14%) were patients over the age of 40 (Table 1).

Sixty percent of our sample presented with psychiatric symptoms causing significant concerns, while 38% reached the threshold for depressive disorder. Among the depressive disorder group, low mood was the major presenting symptom in 32% of cases, with lack of interest occurring in 24%, weight loss in 10%, psychomotor changes in 22%, fatigue in 12%, excessive guilt in 12%, lack of concentration in 28%, severe insomnia in 2%, and suicidal thoughts in 2% Tables 2 and 3.

Most children developed remarkable behavioural abnormalities. On the other hand, 38% of the adult patients in the sample met the criteria for a diagnosis of personality disorder. Twenty-six percent of our patients presented with high social sensitivity and irritability. Resentment featured in 24% of cases, impulsivity was a problem for 14% of our sample, while mistrust and suspiciousness were found in 16%. When all personality traits were categorized according to ICD-10 personality disorders, 15% satisfied the threshold of paranoid personality disorder, 10% featured unspecified personality disorder. Twelve percent of our patients had significant social difficulties leading to social isolation. Most patients with psychiatric symptoms presented simultaneously with neurological abnormalities, with a degree of concordance of 61%. None of our patients displayed psychotic features.

Cognitive impairment remains a landmark feature of WD. Almost fifty percent of our patients showed significant cognitive, (24patints, 48%). Attention deficit was detected in 21 patients (42%), some degree of memory impairment was detected in 13 (26%), a lack of orientation was found in 7 (14%), while 10patients (20%) showed intellectual decline.

Thirty-one patients presented with different neurological features. Parkinsonism was diagnosed in 10 patients (20%), hyperkinesia in 5 (10%), rigidity of limbs in 4 (8%), cerebellar ataxia in 1 (2%), tremors in 21 (42%), dysphagia in 6 (12%), pseudo-smile in 8 (16%), abnormal posture in 8 (16%), dysarthria in 9 (18%) and epilepsy in 3 (6%) patients (Figure 1).

Seventeen patients in this sample presented with hepatic manifestations of different severity, with jaundice observed in 32% of cases, anaemia in 28% and acute hepatic failure in 2% of cases. A bilateral Kayser-Fleischer ring test on slit-lamp was positive in

Table 1: Socio-demographic data.

Age Group	No. (%)	Gender	No. (%)
4-15	19 (38)	Male	31 62.0
16-25	13 (26)		
26-30	11 (22)	Female	19 38.0
41-70	7 (14)		
Total	50 (100)	Total	50 100

Table 2: Categorical psychiatric domains affected by Wilson disease.

Psychiatric disorders	Male	Female	Total No. (%)
Personality Disorders	12	07	19 (38)
Depression	10	09	19 (38)
Cognitive impairment	07	17	24 (48)
Psychotic features	0	0	0 (0)
Total			29 (58)

Table 3: Salient neurology and psychiatric features in WD patients.

Salient Depressive Symptoms	No. %	Personality Trait	No. %	Cognitive Impairment	No. %	Neurological findings	No. %
Low mood	16 32	↑ Sensitivity	13 26	Attention	21 42	Tremors	21 42
Lack of concentration	14 28	↑Emotionality	13 26	Memory	13 26	Abnormal posture	20 40
Lack of interest	17 24	↑Irritability	13 26	General Intellect	10 20	Parkinsonism	10 20
Psychomotor abnormality	11 22	↑Resentment	12 24	Orientation	07 14	Dysarthria	09 18
Increased guilt	06 12	↑Impulsivity	07 14		14	Grinning with Pseudo-smile	08 16
Fatigability	06 12	Mistrust	08 16		16	Dysphagia	06 12
Insomnia	06 12	Poor sociality	06 12		12	Hyperkinesia	05 10
Loss of weight	05 10					Limb rigidity	04 8
Suicidal thoughts	01 2					Athetosis	03 6
						Epilepsy	03 6
						Bradykinesia	02 4
						Cerebellar ataxia	01 2

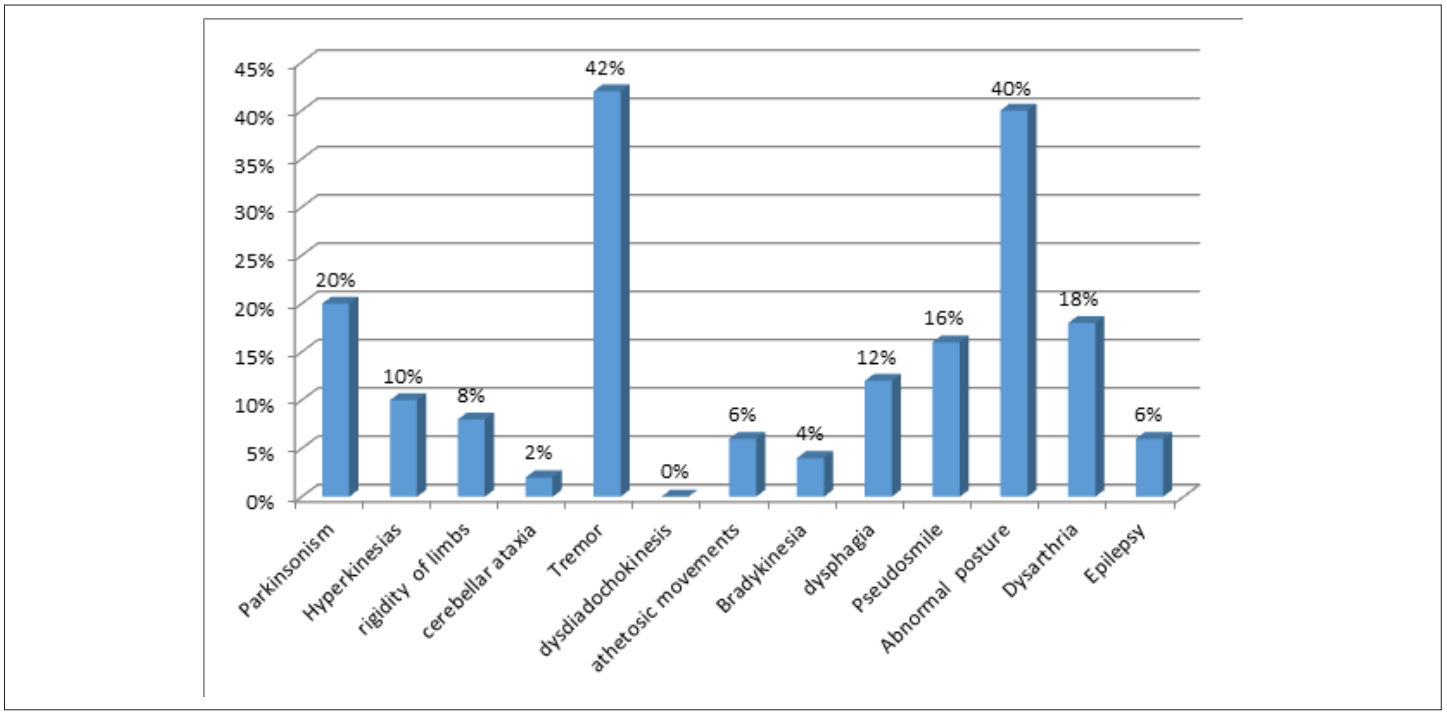

Figure 1: Neurological features.

66% of cases.

DISCUSSION

This study provides detailed neuropsychiatric findings across a heterogeneous population (in terms of age, sex and stage of illness) of patients with WD. The youngest person in the sample was 5 and the oldest was 67, with a mean age of 43±19 years. This is similar to many studies in different European and non-European countries. However, in our sample, despite the wide range of age distribution, we did not identify a single case of late liver function stage, and this may indicate a different prognostic trajectory in Africa in comparison with studies in other countries of European descent [28,32]. This should be re-examined in the future, as our sample is only representative of hospital presentations in the capital city.

Remarkably, 58% of our sample satisfied the ICD 10 criteria for psychiatric disorders, with depression constituting the most frequent disorder, in 19 (38%) case. Likewise, abnormal personality in case of adults and behavioural changes for children, either as comorbid or independent disorder was found in 19 (38%) patients. These figure more than what had previously been reported elsewhere in literature [24,25]. Cognitive impairment was detected in 24 (48%) cases. Although this was mostly due to attention impairment (21, 42%), partly, this was secondary to depression, however, 15 (30%) presented with attention impairment primarily as part of other cognitive impairment directly from the illness diathesis. Sizable number of patients 3 (6%), showed some form of cognitive decline (as per school records and MMSE) in contrast to other reports elsewhere [24,25,33]. We could not detect any evidence of psychosis, perhaps in part because there were no cases of encephalopathy of any sort which could culminate into organic psychosis, as has been reported in many countries [19,20,33]. Other reasons for the lack of psychosis detected in our study include the short length of the study period, being a cross sectional study.

Over 42% of patients with WD presented with minor to severe neurological symptoms. Often, tremors and minor posturing abnormalities (20, 40%) are overlooked, however, severe disorders, such as secondary Parkinsonism, occurred in 10 cases (20%), similar to many other studies reported elsewhere. Severe dystonia, with disabling dysphagia and dysarthria, were found in 8 patients (16%) of our sample. In contrast to previous reports [11-14], in this study dysdiadochokinesis did not feature in any of our cases. Only a few of our patients presented with major cerebellar symptoms and signs [33].

CONCLUSION

Although the predominant manifestations and prevalence of WD are similar worldwide, we believe the trajectory of the illness, with its predilection features, possibly, has regional and ethnical differences. This study highlights some significant findings in the neuropsychiatric domains, especially in relation to higher rate of psychiatric and personality and behavioural disturbances in the course of WD. Moreover, there is some evidence to indicate a less aggressive course in relation to liver failure. Long-term prospective study is recommended to confirm initial findings.

LIMITATIONS

This cross-sectional study implicitly carries some limitations. It is unable to relate the emergence of the various symptoms to the stage of the illness. Likewise, is not controlled with comparative cases. Inherently, the study was not meant to answer the relationship of symptoms to treatment agents. Moreover, most cases were not confirmed via genetic studies due to limited resources, similar to many low income settings. We also recommend more sensitive scale for measuring children's behavioural problems in the any future study.

DECLARATIONS

Ethics and consent to participate

The study was approved by the Sudanese Medical Specialisation Board, reference number is not applicable. Written permission was obtained from administration departments of the hospitals. Written informed consents were obtained from all participants and their parents in cases of minors.

Consent for publication

Not applicable.

Availability of data and materials

The dataset used and analysed in this research is available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

Not applicable.

Authors contributions

H.J.E. made substantial contributions to the conception of the study and was responsible for data acquisition. A.O. and Y.O.Y. provided supervision and guidance throughout all phases of the study. A.O. drafted the article. All authors provided critical revisions regarding important intellectual content and approved the final version.

REFERENCES

1. Ferenci P. Regional distribution of mutations of the atp7b gene in patients with Wilson Disease: Impact on genetic testing. Hum Genet. 2006; 120:151-9.
2. Bull PC, Thomas GR, Forbes J, Rommens JM, Cox DW. The Wilson Disease gene is a putative cooper transporting p-type ATPase similar to Menkes gene. Nat Genet. 1993; 5:327-37.
3. Wilson SA. Progressive lenticular degeneration: A familial nervous disease associated with cirrhosis of the liver. Brain 1912; 34: 20–509.
4. Bem RS, Muzzillo DA, Deguti MM, Barbosa ER, Werneck LC, Teive HA. Wilson's disease in southern Brazil: A 40-year follow-up study. Clinics 2011; 66(3):411-6.
5. Dusek, P, Litwin, T, Czlonkowska, A. Wilson disease and other neurodegenerations with metal accumulations. Neurol Clin. 2015; 33: 175–204.
6. Matarazzo EB. Psychiatric features and disturbance of circadian rhythm in Wilson disease. The Journal of Neuropsychiatry and Clinical Neurosciences. 2002; 14:335-339.
7. Lai CH, Tseng HF. Department of Neurology, Changhua, Taiwan Population-based epidemiologic study of Wilson's disease in Taiwan. Eur J Neurol. 2010; 17:830-3.
8. Litwin, T, Dzieżyc K, Karliński M. Psychiatric disturbances as a first clinical symptom of Wilson's disease. PsychiatrPol 2016; 50: 337–344.
9. Hermann W. Classification and differential diagnosis of Wilson's disease. Annals of Translational Medicine. 2019; 7:63.

10. Gow PJ, Smallwood RA, Angus PW, Smith AL, Wall AJ, Sewell RB. Diagnosis of Wilson's disease: An experience over three decades. 2000; 46:415–419.

11. Portala K, Westermark K, Ekselius L, Von Knorring L. Personality traits in treated Wilson's disease determined by means of the Karolinska Scales of Personality (KSP). Eur Psychiatry 2001; 16: 362–371.

12. Lin JJ, Lin KL, Wang HS, Wong MC. Psychological presentations without hepatic involvement in Wilson disease. Pediatr Neurol. 2006; 35: 284–286.

13. Jackson GH, Meyer A, Lippmann S. Wilson's disease: Psychiatric manifestation may be the clinical presentation. Postgrad Med 1994; 95: 135–138.

14. Merle U, Schaefer M, Ferenci P, Stremmel W. Clinical presentation, diagnosis and long-term outcome of Wilson's disease: A cohort study. Gut. 2007; 56:115-20.

15. Machado AAC, Chien HF, Deguti MM, Genschel J, Cançado E, Bochow B, et al. Neurological manifestations in Wilson's disease: Report of 119 cases. Mov Disord. 2006; 21:2192-6.

16. Ferenci P, Caca K, Loudianos G, Mielli-Vergani G, Tanner S, Sternlieb I, et al. Diagnosis and phenotypic classification of Wilson Disease. Liver Int. 2003; 23:139-42.

17. Shribman S, Warner TT, Dooley JS. Clinical presentation of Wilson disease. Ann Transl Med. 2017; 7:S60.

18. Zimbrean PC, Schilsky ML. The spectrum of psychiatric symptoms in Wilson's disease: Treatment and prognostic considerations. AmJ Psychiatry 2015; 172: 1068–1072.

19. Litwin T, Dusek P, Szafranski T, Dziezyc K, Czlonkowska A, Rykakowsku JK. Psychiatric manifestation in Wilson's disease: Possibilities and difficulties for treatment. Ther Adv Psychopharmacol. 2018; 8:199–211.

20. Rubinstein SS, Young AB, Kluin K, Hill G, Aisen AM, Gabrielsen T, et al. Clinical assessment of 31 patients with Wilson's Disease. Correlations with structural changes on magnetic resonance imaging. Arch Neurol. 1987; 44:365-70.

21. Strickland GT, Leu ML. Wilson's Disease: Clinical and laboratory manifestations in 40 patients. Medicine. 1975; 54:113-37.

22. Beinhardt S, Leiss W, Stattermayer AF. Long term outcomes of patients with Wilson disease in large Austrian cohort. Clin Gastroenetrol Hepatol. 2014; 12: 683–689.

23. Mura G, Zimbrean PC, Demelia L. Psychiatric comorbidity in Wilson's disease. Int Rev Psychiatry 2017; 29: 445–462.

24. Zimbrean P, Seniow J. Cognitive and psychiatric symptoms of Wilson disease. Hand Clin Neurol. 2017; 142:121–40.

25. Denning TR, Berrios G. Wilson's disease psychiatric symptoms in 195 cases. Arch Gen Psychiatry 1989; 46: 1126–1134.

26. Carta MG, Mura G, Sorbello O. Quality of life in psychiatric symptoms in Wilson's disease: The relevance of bipolar disorders. Clin Pract Epidemiol Ment Health 2012; 8: 102–109.

27. Sahoo MK, Avasthi A, Sahoo M, Modi M, Biswas P. The Psychiatric manifestations of Wilson's disease and treatment with electroconvulsive therapy /Indian J Psychiatry. 2010; 52: 66–68.

28. Bruha R, Marecek Z, Pospilova L. Long-term follow-up of Wilson disease: Natural history, treatment, mutations analysis and phenotypic correlation. Liver Int. 2011; 31: 83–91.

29. World Health Organization. The ICD-10 classification of mental and behavioural disorders: Clinical descriptions and diagnostic guidelines. Geneva: World Health Organization; 1992.

30. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Washington, DC: Author; 1994.

31. Sorbello O, Riccio D, Sini M, Carta M, Demelia L. Resolved psychosis after liver transplantation in a patient with Wilson's disease. Clin Pract Epidemiol Ment Health. 2011; 7: 182–184.

32. Azova S, Rice T, Discussants, Garcia-Delgar B, Coffey BJ. New-onset psychosis in an adolescent with Wilson's disease. J Child Adolesc Psychopharmacol. 2016; 26: 301–304.

33. Srinivas K, Sinha S, Taly AB, Prashanth LK, Arunodaya GR, Reddy YJ, et al. Dominant psychiatric manifestations in Wilson's disease: Diagnostic and therapeutic challenge. J Neurol Sci 2008; 266: 104–108.