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SHORT COMMUNICATION

Wilson's Disease: Experience at a Tertiary Care Hospital

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ABSTRACT

Wilson's disease (WD) is a rare autosomal recessive disorder of copper metabolism. Data regarding WD is not available from Pakistan. A cross-sectional study was conducted at The Aga Khan University Hospital, Karachi, and all patients admitted with primary and secondary diagnosis of Wilson's disease were added. A total of 47 patients were seen; 68% (n = 32) were male. The mean age was 26.6 ± 9.97 years. Most of the patients presented with hepatic, (n = 22, 46.8%), neurological, (n = 17, 36.2%) and psychiatric (n = 8, 17%) symptoms. Mean ceruloplasmin level was 0.17 ± 0.13 g/dl; it was < 0.25 g/dl in 39 (86.6%) patients. Serum copper (Cu) was reduced in 32 (68.1%) patients and 24-hr-urinary Cu was raised in 22 (47.6%) patients. Slit lamp examination for Kayser-Fleischer (KF) rings was done on 15 (31.9%) patients and 9 (60%) of them had KF rings. Mean serum aspartate transaminase (AST) / alanine transaminases (ALT) ratio was 1.92 and median alkaline phosphatase / total bilirubin ratio was 79.30 (IQR 35.05; 166.50).

Key Words: *Wilson's disease. Kayser-Fleischer (KF) ring. Serum copper.*

Wilson's disease (WD) is a rare autosomal recessive disorder of copper metabolism, caused by decreased biliary copper excretion and deposition in liver, brain, kidneys and skeletal system. The patients present with a variety of clinical symptoms, the most common being liver disease, neurological and psychiatric disturbances.[1,2] The diagnosis of WD is difficult because of lack of specific and sensitive tests for WD. Due to relative rarity of WD and lack of awareness among the physicians, this disease is not diagnosed early, at least in our country. Therefore, majority of patients present late with either decompensated liver disease or incapacitating neurologic disease.[3] To the best of the authors' knowledge, there is very limited data and available literature on WD from Pakistan,[4] so a cross-sectional study was done at The Aga Khan University Hospital, Karachi. After data collection and analysis, a comparison with studies from India, Japan and Europe was made.[5-7]

A total of 47 patients were seen from 1985 to 2011, and 32 (68.1%) among them were male. The mean age of the patients was 26.6 ± 9.97 years. The most common presentation in this group of patients was hepatic, (n = 22, 46.8%), followed by neurological, (n = 17, 36.2%) and psychiatric (n = 8, 17%) patients. The patients with psychiatric symptoms had an earlier onset of disease at the mean age of 18.8 ± 3.3 years.

The clinical diagnosis of WD was confirmed with ceruloplasmin level, 24-hour-urinary copper and serum copper level (Table I). The two ratios (SGOT/SGPT, Alk.P/T.Bil) which had been recently reported in a study in acute liver failure patients were also calculated. The mean value for AST/ALT ratio was 1.92 ± 1.36 and median value for Alk.P/T.Bil ratio was 79 (IQR 35.05; 166.50). MRI was done in 21 (84%) patients of neuropsychiatric group and 17 (81%) of these were found to have abnormal signaling within basal ganglia, consistent with WD.

Table I: Diagnostic investigations for WD.

[1]Ceruloplasmin levels (g/dl)	0.17 ± 0.13
[2]24-hr urinary copper secretion* (ug/day)	155 (IQR 44.26; 407.75)
[3]Serum copper (ug/dl)*	55.60 (IQR 34.42; 73.75)
AST/ALT ratio	1.92 ± 1.36
Alkaline phosphatase/ total bilirubin ratio*	79.30 (IQR 35.05; 166.50)

** Median with interquartile ranges (IQR) has been reported for these variables*
1. normal values > 0.25g/dl, 2. normal values (70-160µg/dl) 3. Normal values 70-160µg/dl

The mean age at onset was slightly higher in this cohort as compared to other comparison studies. There was a higher burden of WD in male population, which is quite comparable with studies from India and Japan, but European study on the other hand had shown a higher female predominance (Table II). The most common mode of presentation in this cohort was hepatic, which is consistent with Japanese and European studies.[5,7] Data from Indian study, however, has reported a high predominance of neuropsychiatric symptoms and a lower mean age-of-onset.[6] This has also been observed in the present study that psychiatric mode of presentation was more common in younger age group with a mean age of presentation at 18.8 ± 3 years.

The diagnostic biochemical parameters in this study showed low ceruloplasmin levels in most of our patients. For those tested for 24-hr-urinary copper, less than half had raised levels. This is comparable with results from Japanese study, but on the contrary, studies from India and Europe had shown very high percentage of patients with raised 24-hr-urinary Cu levels. Similar trends were

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Table II: Comparison of WD in Pakistan, India, Japan and European countries.

	Pakistan	India (6)	Japan (7)	European countries (5)
Year	2011	2007	2010	2007
Study period	1985-2011	1970-2000	1999-2007	2000-2005
Place of study	Karachi, Pakistan	Bangalore, India	Nagoya and Kanazawa, Central Japan	Heidelberg, Germany
Number of cases	47	282	30	163
Male: Female	32:15	196:86	20:10	65:98
Prevalence of males	68%	69%	66.6%	39.8%
Mean age at onset (years)	26.6 (mean age at presentation)	15.9	17.5	17.4
Symptoms				
Hepatic	22 (46.8%)	42 (14.9%)	22 (73.3%)	96 (58.9%)
Neurological	17 (36.2%)	195 (69.2%)	5 (16.7%)	55 (33.7%)
Psychiatric	8 (17%)	7 (2.48%)		
Other (i-e musculoskeletal, hemolytic or mixed symptoms)		38 (13.55%)	3 (10%)	12 (7.4%)
Diagnostic tests				
Ceruloplasmin levels	Reduced in 86.6%	Reduced in 88%	-	Reduced in 88.2%
Serum copper	Reduced in 68.1%			
Hepatic copper output				High in 92.7%
24-hr urinary copper excretion	Raised in 47.6%	Raised in 96%	Raised in 36.4% with hepatic form and 40% with neurological form	Raised in 87.1%
KF ring				
In hepatic form	Present in 28.6%	Present in 13.6%	Present in 41%	Present in 52.1%
In neurological form	Present in 87.5%	Present in 100%	Present in 100%	Present in 85.5%

seen in ophthalmological examination with KF rings, which were present in almost all patients with neurological symptoms in all studies. However, the presence of KF rings in patients with predominantly hepatic symptoms varied in these studies.[8]

WD should be suspected in patients who have unexplained abnormal liver function tests and whose family history is positive for liver disease. Due to similar patterns of biochemical parameters in WD in all these different regions and due to high percentage of hepatic presentation in our country, a clinician should check for atleast three values in case of unexplained liver disease; namely (i) low ceruloplasminemia (ii) high 24-hr-urinary copper (iii) presence of KF rings on ophthalmic examination.

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