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CLINICAL SPECTRUM OF WILSON'S DISEASE, A CROSS-SECTIONAL ANALYSIS FROM A TERTIARY CARE HOSPITAL IN KARACHI

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Abstract

Wilson's Disease (WD) is an autosomal recessive disorder of copper metabolism with psychiatric, neurological, and hepatic manifestations. It can be diagnosed early, but most of the time, it is delayed, especially in developing countries like Pakistan where genetic testing is still unavailable. This paper fills a gap in knowledge by comparing 300 WD-diagnosed patients who presented at Abbassi Shaheed Hospital, Karachi, on the basis of the EASL 2012 criteria. The investigation sought to establish the clinical and biochemical range of WD and identify statiscal significant diagnostic markers. Data analysis employed SPSS v20. The most common presentation was hepatic (45%), then neurological (40%) and psychiatric (10%). 78% had Kayser-Fleischer rings, which was the largest group among neurologically symptomatic patients. 85% had low ceruloplasmin and 88% urinary copper excretion. Statistically significant correlations between clinical category and KF ring presence ($\chi^2 = 35.2$, $p < 0.001$) and between clinical group and ceruloplasmin level ($F = 12.45$, $p < 0.001$) were present. These data favor the application of biochemical and ocular markers in developing countries and validate early multidisciplinary diagnostic strategies.

INTRODUCTION

Wilson's Disease (WD), also scientifically referred to as hepatolenticular degeneration, is an uncommon but serious inherited metabolic disorder first described and identified in 1912 by neurologist S.A.K. Wilson. The disease is caused by mutations in the ATP7B gene, with an autosomal recessive pattern of inheritance. The gene codes for an essential copper-transporting ATPase enzyme involved in the incorporation of copper into ceruloplasmin and its excretion into bile. When mutations disrupt the function of ATP7B, copper tends to accumulate excessively in the body, mostly affecting organs like the liver, brain, and cornea. This copper accumulation progresses to cause massive cellular toxicity and tissue damage, which finds expression in different clinical symptoms based on the site and degree of accumulation (Roberts & Schilsky, 2008; De Bie et al., 2007).

Globally, Wilson's Disease is estimated to occur in about 1 in 30,000 individuals, while heterozygous carrier frequency is about 1 in 90 persons (Ala et al., 2007). It is probably underestimates in those areas where consanguinity is practiced, e.g., South Asia, i.e., Pakistan and India. Such populations have a higher incidence of autosomal recessive disorders because of enhanced genetic homogeneity from intermarriage among related persons (Naseer et al., 2020). Clinical presentation of WD varies very significantly and significantly from one patient to another. The variability is responsible for delay in diagnosis. It may

present in early childhood, adolescence, or even early adulthood with signs from asymptomatic elevation of hepatic enzymes to outright failure of the liver, psychiatric syndromes (e.g., depression, anxiety, or personality alterations), and slowly progressive neurological deterioration such as tremors, rigidity, dystonia, and dysarthria (Merle et al., 2007). These diverse presentations often result in misdiagnosis or underdiagnosis until disease is well beyond an early, potentially reversible phase.

Pakistan has a wide gap in the epidemiological information regarding Wilson's Disease. The information available is based mostly on small-scale institutional case series and individual clinician impressions, which potentially do not reflect the larger population-level disease burden (Parkash et al., 2013). No large-scale, national studies have been performed to date to determine the true prevalence, clinical patterns, or outcomes related to WD within the nation. This deficiency of integrated data handicaps both effective clinical diagnosis and long-term management strategies, as well as planning of public health policy and allocation of resources. Hence, the present study attempts to overcome these deficiencies by systematically examining the demographic trends, clinical presentations, and biochemical markers of Wilson's Disease in a large cohort from a public sector tertiary care hospital. A systematic and statistically rigorous approach will be employed to provide strong and significant results that can guide both clinical practice and future studies.

Methods

This cross-sectional study was undertaken at the Neuro medicine Department of Abbassi Shaheed Hospital, Karachi, during January to July 2023. Ethical permission was obtained from the Institutional Review Board of the hospital. On the basis of hospital records and feasibility, a target sample of 300 patients was chosen. All the patients were diagnosed based on EASL 2012 criteria: hepatic involvement plus two or more of the following – low ceruloplasmin (<20 mg/dL), increased 24-hour urinary copper (>100 μg), KF rings, or family history. Information was obtained on a standardized and validated proforma. Laboratory investigations involved serum ceruloplasmin (quantitated through nephelometry), serum copper, 24-hour urinary copper (colorimetric assay), and liver function tests. Examination by slit-lamp was performed by a qualified ophthalmologist. Anthropometric information and clinical signs were obtained by neurologists experienced with movement disorders. Information was checked and entered twice.

Analysis was conducted using SPSS v20. Descriptive statistics provided frequencies and distributions. Chi-square tests were employed to evaluate associations between categorial variables. One-way ANOVA evaluated differences between ceruloplasmin levels in clinical groups, with post hoc analysis via Tukey's HSD. Pearson's correlation coefficient was employed to investigate relationships between ceruloplasmin and severity of symptoms.

Results

The sample included 174 men (58%) and 126 women (42%) with a mean age of 22.4 years (± 8.9 SD). The sample included 70% of the people less than 25 years old. The greatest proportion of the sample was Sindhi (65%), followed by Punjabi (20%), and others (15%). The educational data revealed that 70% of the sample had not completed matriculation yet, which means most were of low socioeconomic status.

Jaundice, hepatomegaly, and elevated transaminases were hepatitic manifestations in 135 (45%) of the patients. Neurological manifestations as tremor, dystonia, and gait impairment were observed in 120 (40%) of the patients, and psychiatric presentations such as depression and personality change were observed in 30 (10%) of the patients. Fifteen (5%) were asymptomatic, often detected during family screening.

Kayser-Fleischer rings were present in 234 patients (78%). KF ring prevalence varied among clinical categories: neurological (85%), psychiatric (83%), hepatic (55%), and asymptomatic (47%).

Table 1. Clinical Presentation of Wilson's Disease Patients

Clinical Category	Frequency (n=300)	Percentage (%)
Hepatic	135	45.0

Neurological	120	40.0
Psychiatric	30	10.0
Asymptomatic	15	5.0

Table 2. Laboratory Findings (Mean ± SD)

Parameter	Mean ± SD	Normal Range
Serum Ceruloplasmin (mg/dL)	14.5 ± 5.2	20 - 40
Serum Copper (µg/dL)	45.3 ± 15.1	70 - 140
24-Hour Urinary Copper (µg)	150.2 ± 40.5	<100

The chi-square test was significant for association between clinical category and KF ring presence (χ^2 = 35.2, df = 3, $p < 0.001$). ANOVA results indicated statistically significant differences in ceruloplasmin levels among clinical groups ($F = 12.45$, $p < 0.001$). Post hoc Tukey tests confirmed significantly reduced ceruloplasmin levels in the neurological and psychiatric groups compared to the hepatic group. Pearson's correlation coefficient found a moderate inverse relationship between ceruloplasmin levels and neurological severity ($r = -0.54$, $p < 0.01$).

Discussion

The findings are consistent with previously established worldwide data that hepatic and neurological manifestations are the major presentations of Wilson's Disease (Ala et al., 2007; Merle et al., 2007). The comparatively high proportion of neurologically symptomatic patients relative to Western cohorts may be due to delayed diagnosis because of absence of routine hepatic screening and reduced awareness by general practitioners. KF rings were found most sensitive in neurologically affected patients, confirming their diagnostic utility (Rosencrantz & Schilsky, 2011). The biochemical results, particularly low ceruloplasmin levels, are in keeping with ATP7B pathophysiology. The substantial group differences confirm the clinical usefulness of ceruloplasmin for diagnosis and potentially for assessing disease severity. The raised urinary copper levels are in keeping with earlier diagnostic research and indicate copper overload (Gow et al., 2000).

This research emphasizes the necessity of greater awareness among clinicians, especially in primary care, and promotes the inclusion of WD screening in unexplained hepatic or psychiatric symptomatology in patients. The analysis of correlation also hails ceruloplasmin as a low-cost monitoring modality in follow-up management.

Limitations

Even with its strengths, this study is also limited by single-center design and absence of genetic confirmation of ATP7B mutations. While sample size was large, subgroup comparisons (e.g., by gender or age strata) potentially remain underpowered. Recall bias and the lack of standardized neuroimaging or psychiatric rating scales potentially affected symptom classification.

Conclusion

This work provides critical data regarding the clinical and biochemical presentation of Wilson's Disease in a Pakistani tertiary care environment. Hepatic presentation is still most frequent, but neurological and psychiatric presentations are common and diagnostically revealing. Kayser-Fleischer rings and ceruloplasmin are still key in the diagnosis in resource-limited settings. There is an urgent need for national guidelines to include WD screening as part of hepatic and psychiatric evaluation protocols.

Future research should involve molecular genetic testing and long-term follow-up to further elucidate genotype-phenotype correlations and response to therapy.

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