



WILSON'S DISEASE; NEUROLOGICAL MANIFESTATIONS IN PATIENTS PRESENTING TO TERTIARY CARE FACILITY

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INTRODUCTION

Wilson's disease is an inherited autosomal recessive disorder in which defective biliary excretion of copper leads to its accumulation, particularly in the liver & Cornea and other sites in the body, most notably the central nervous system.¹ Although Wilson's disease is extremely rare in clinical practice, it is important because it is often fatal if not recognized and treated when symptomatic. Often, the diagnosis is not made until adulthood, despite manifestations of the disease beginning to develop in childhood.²⁻⁴

Neurologic Wilson's disease most frequently becomes symptomatic in late childhood through early adulthood with a mean age of onset between 15 and 21 years of age. Symptoms, clinical course and outcome of Wilson are highly variable. In principle, the main features – the hepatic and the neurologic form- can be distinguished, but many patients present with a mixture of both. The

ABSTRACT... Objectives: To determine the frequency of various neurological manifestations of Wilson's disease in patients presenting to tertiary care facility. **Study design:** Cross sectional study. **Setting:** Neurology ward, JPMC, Karachi. **Period:** 14-03-2012 to 13-09-2012. **Patients and Methods:** A total of 150 diagnosed patients of Wilson's disease between the age 15 and 55 years were recruited. Structured questionnaire was used to collect the data regarding neurological manifestations of Wilson's disease along with slit lamp examination for kayser-Fleischer rings. Data were entered and analyzed in SPSS version 17. Chi-Square test was used as test of significance. **Results:** Mean age + S.D of patients was 38.7 + 8.23 years. Most of the patients (42%) belongs to age between 41 to 50 years. Male to female ratio was 2:1. Tremor was the most common neurological manifestation (88.7%) followed by dysarthria in 77.3%, dystonia was present in 59.3%, chorea in 36%, and Parkinsonism in 28.7%. All patients had the Kayser-Fleischer ring positive. Upon stratification of gender, tremor & dysarthria were more common in males as compared to females. Only dysarthria was significantly noted to increase with increasing age up to 5th decade of life and decreased after age of 51 years. (P value < 0.001). **Conclusion:** Neurologic manifestations are very common in patients of Wilson's disease, tremor being the most common with male predominance.

Key words: Wilson's disease, Neurologic manifestations.

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neurologic form is variable¹ and characterized by cumulative motor dysfunction. Initial symptoms are often unspecific, mild and may not be recognized. Clinical signs include asymmetric distal accentuated tremor, 'wing beating' tremor, intention tremor, and sometimes tremor of the trunk and head. Rigidity, dystonia and bradykinesia can be observed as well as dysarthria, dysphagia and difficulties with writing.⁵⁻⁷

The aim behind this study was to determine the neurological manifestations of Wilson's disease in patient presenting to tertiary care facility.

PATIENTS AND METHODS

This is a descriptive hospital based study carried out in the department of Neurology, Jinnah Postgraduate Medical Centre (JPMC), Karachi between the periods of six months from 1st March 2011 to 30th September 2014.

We have evaluated a total of 150 patients those who were admitted in the Neurology ward as a diagnosed case of Wilson's disease between the ages of 15 - 50 years of either sex. Consent was taken from the patient. A detailed history was taken and thorough examination was performed regarding neurological manifestation of Wilson's disease such as slow and slurred speech, tremors at rest, slow voluntary movements and abnormal posture were recorded. Patient was also sent to ophthalmology department for slit lamp examination for Kayser-Fleischer (K.F ring). All the related data was collected on a questionnaire.

A preformed structured questionnaire was used to collect the relevant data such as age, gender, area of residence, marital status, Body Mass Index (BMI), weight, outdoor eating habit, cigarette smoking, blood sugar levels, and blood pressure levels.

DATA ANALYSIS

All the data was entered and analyzed in SPSS version 17. Descriptive statistics were used to summarize the continuous data variable like age and presented as mean \pm SD; while categorical variables were reported as percentages and frequencies of dysarthria, dystonia, tremors, chorea, Parkinsonism, Kayser-Fleischer ring and gender. Stratification were made to control

confounding variables on these outcomes by age and gender through Chi-Square test with P value <0.05 taken as significant.

RESULTS

Mean age \pm S.D of patients was 38.7 ± 8.23 years with predominantly males (67.3%) than females (32.7%) and a male to female ratio was 2:1. Upon categorization of ages of patients; most common age group was 31 to 40 years (42%).

The most common neurological manifestation among patients with Wilson's disease was presence of tremor (88.7%) and the least common was Parkinsonism which was found in 28.7% of patients. It was noted that all the 150 patients (100%) had the Kayser Fleischer (KF) rings positive on slit lamp examination. Figure-1.

When stratification of gender was made it was noted that tremor and dysarthria were more common in males than females but they did not achieved statistical significant value, (90.1% and 85.7%, P value 0.631) and (79.2% and 73.5%, P value 0.620). Frequency of dystonia, chorea, and Parkinsonism and Kayser Fleischer ring was almost equal in both genders. The above stated three findings were statistically significant. (P value <0.001 , 0.541 & <0.001). Table-I.

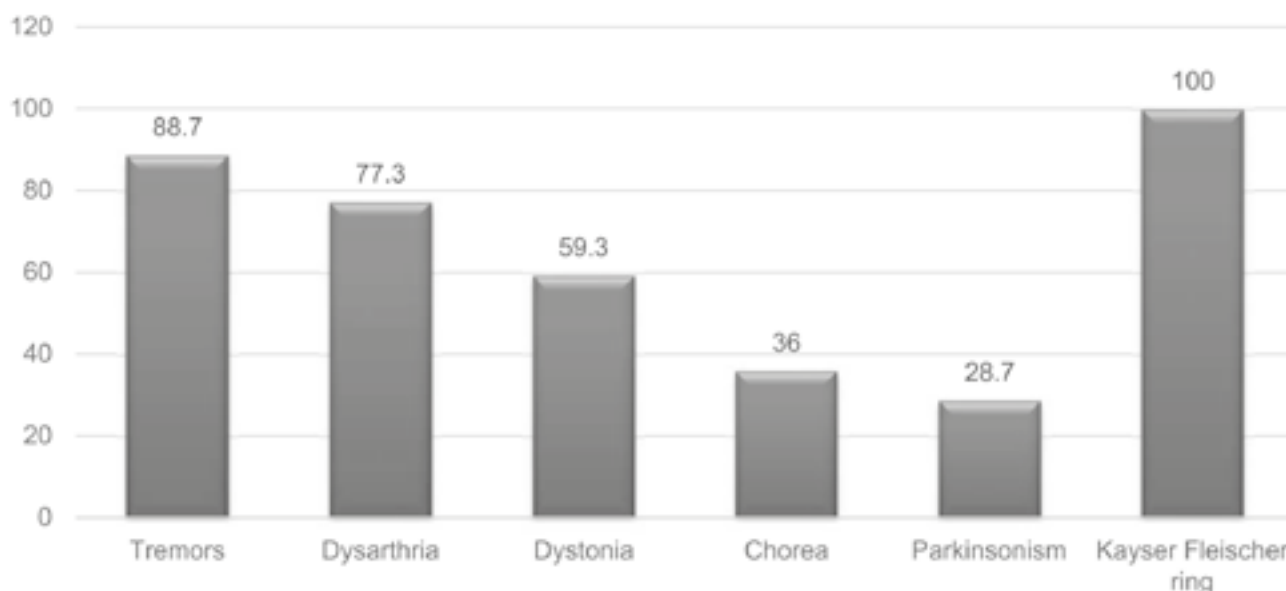


Figure-1. Frequencies of Various Neurological Manifestations of Patients of Wilson's disease

Upon stratification of age into categories followed by analysis it was seen that frequency of tremor, dystonia, chorea and Parkinsonism was variable and did not show any specific pattern and there were no significance of the finding. Only dysarthria was significantly noted to increase with increasing age up to 5th decade of life and decreased after age of 51 years. (P value <0.001). Kayser Fleischer ring positive in all patients of any age category. Table-II.

DISCUSSION

Main target organs of Wilson's disease in the human body are Liver, cornea, and Brain. The initial presentation of Wilson's disease may be vague and can be simulated and confused with other disease of these both systems. With passage of time and disease progression the diagnosis becomes clear.⁸

Mean age of our patients was 37.78 ± 8.23 years. This study included patients of age from 15 years

Neurological manifestation	Gender wise frequency		Totals n= 150	P value
	Male (n=101)	Female (n=49)		
Tremors	91 90.1%	42 85.7%	133 88.7%	0.631
Dysarthria	80 79.2%	36 73.5%	116 77.3%	0.620
Dystonia	60 59.4%	29 59.2%	89 59.3%	<0.001
Chorea	37 36.6%	17 34.7%	54 36.0%	0.054
Parkinsonism	29 28.7%	14 28.6%	43 28.7%	< 0.001
Kayser Fleischer ring	101 100.0%	49 100.0%	150 100.0%	-

Table-I. Gender Wise Frequency & Percentage of Various Neurological Manifestations of Patients of Wilson's Disease
P value <0.05 taken as significant.

Neurological manifestations	Age category wise Frequency & Percentage				Totals (n = 150)	P value
	≤ 30 years (n = 30)	31 to 40 years (n = 50)	41 to 50 years (n = 63)	≥ 51 years (n = 7)		
Tremors	27 90.0%	45 90.0%	57 90.5%	4 57.1%	133 88.7%	< 0.064
Dysarthria	22 73.3%	38 76.0%	54 85.7%	2 28.6%	116 77.3%	< 0.006
Dystonia	17 56.7%	33 66.0%	38 60.3%	1 14.3%	89 59.3%	< 0.074
Chorea	15 50.0%	17 34.0%	19 30.2%	3 42.9%	54 36.0%	< 0.294
Parkinsonism	8 26.7%	15 30.0%	18 28.6%	2 28.6%	43 28.7%	< 0.992
Kayser Fleischer ring	30 100.0%	50 100.0%	63 100.0%	7 100.0%	150 100.0%	-

Table-II. Age category wise frequency & percentage of various neurological manifestations of patients of wilson's disease.
P value <0.05 taken as significant

to 55 years; while Machado A and coworkers in an earlier study investigated neurological manifestation in patients with Wilson's disease and found the mean age 19.6 years ranging from 7 to 37 years.⁹ This difference was due to study design. Beside that long survival due to early diagnosis and treatment in our patients (most of which were living in Karachi) could also have produced this difference of ages. Still in the current study 20% of participants were below 30 years which also suggests that neurological manifestations are common in lower age patients in urban areas like Karachi as well. In a study Burke JF, et al;¹⁰ found that of all Wilson's disease patients with neurological manifestations, irrespective of their follow up status the mean age \pm SD was 39 ± 15 years.¹ While another study documented the range of 45-55 years as common ages when these patient lately present with neurological manifestations.

In current study the tremor was most common neurological manifestation and was present in 88% patients. Khan A and coworkers also found similar results i.e. 86.7%. In a previous studies tremor was also seen to be the most prevalent neurological manifestation while there was much variability in frequency of other neurological manifestations of Wilson's disease.^{11,12}

Upon age stratified analysis it was seen that all the neurological manifestations were less frequent in elder than 51 years age group. Dysarthria was up to one third less in mentioned age group as compared to younger ages (p value = 0.006). It is reasonable to think that this was due to timing of presentation & duration of Wilson's disease.

Although Kayser-Fleischer rings are a useful diagnostic sign, they are no longer considered pathognomonic of Wilson disease unless accompanied by neurologic manifestations.¹³ Kayser-Fleischer ring is deep ring appearing in cornea at its periphery. The ring is of greenish gold to brown color; when well developed, ring may be readily visible to the naked eye or with an ophthalmoscope on slit lamp examinations. Some studies document that Kayser-Fleischer

rings are present in 95-100% of patients with neurological symptoms, in 50-60% of patients without neurological symptoms and in only 10% of asymptomatic siblings.¹⁴ The current study found that it was present in all patients (100%).

This study was a hospital based study where many patients were follow-up cases and were on treatment since many years. This could have affected the mode of presentation and frequency of different neurologic manifestations in them. As the study focused on frequency of neurologic manifestations in Wilson's disease patients therefore diagnostic laboratory and radiological findings were out of the scope of this study.

CONCLUSION

Neurologic manifestations (tremor, dysarthria, dystonia, chorea, Parkinsonism) are very common in patients of Wilson's disease, tremor being the most common. Male gender is more affected than females. Wilson's disease should be considered in any individual of any age having with liver and neurological abnormalities of uncertain cause.

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“You have to believe in yourself
when no one else
does that makes you a winner right there.”

Venus Williams



AUTHORSHIP AND CONTRIBUTION DECLARATION

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