ORIGINAL RESEARCH PAPER
Volume - 9 | Issue - 7 | July - 2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A STUDY ON WILSON'S DISEASE IN EASTERN INDIA

General Medicine

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ABSTRACT

Wilson's disease is an inherited neuro-metabolic disorder with an estimated prevalence ranging from one in 30000 to one in 100000, but it is perhaps more commonly found in India.[1-2]It is a disorder of copper metabolism transmitted by a mutated gene, present on chromosome 13q14.3. As our clinical, biochemical, histological, radiological and genetic understanding of the disease has improved, Wilson's disease which is invariably fatal, if left untreated, has now become controllable with proper treatment. This study puts in an effort to study the varied presentations of patients suffering from Wilson disease in Eastern India.

KEYWORDS

INTRODUCTION:

Wilson's disease, also known as hepatolenticular degeneration or Westphal-Strumpell Pseudosclerosis, is an inherited autosomal recessive disorder of hepatic copper metabolism leading to copper accumulation in hepatocytes and in extrahepatic organs such as brain, kidneys and cornea.[3]The gene, ATP7B, present on chromosome 13q14.3, codes for a membrane bound, copper binding ATPase. The disease occurs due to multitude of mutations within this gene. The mutation gives rise to two fundamental disturbances of copper metabolism:[4]

(1) A reduced rate of incorporation of copper into ceruloplasmin, and
(2) A reduction in biliary excretion of copper.

Since intestinal absorption is normal in Wilson's disease, there is a substantial positive copper balance in the body.[5-6]

The onset of neurologic symptoms is usually in the second decade. In childhood, the liver disorder often takes the form of attacks of jaundice, unexplained hepatospleenomegaly, or hyperspleenism with thrombocytopenia and bleeding. The hepatic abnormalities may be asymptomatic, in which case the initial clinical presentation is neurologic.[7] Such patients, predominantly present with extra-pyramidal symptoms like tremor and bradykinesia. "Classic syndrome" typically involves facial and bulbar muscles resulting in dysarthria, dysphagia, hoarseness of voice and fixity of facial muscles with mouth constantly agape. Psychiatric features like emotional liability, impulsiveness, psychosis and depression may also be noted in few patients of Wilson's disease.

In some patients, the initial presenting feature may be a hemolytic anemia or renal tubular acidosis.

Kayser-Fleischer rings (crescentic rusty-brown discoloration of Descemet membrane) may not be evident in initial stages of Wilson's disease, but is almost invariably present once neurologic signs appear.

Wilson's disease in Eastern India, as anywhere else, has protean manifestations. Children with slow onset extra-pyramidal syndrome should always be investigated thoroughly to exclude Wilson's disease. Screening of all asymptomatic siblings of a patient with Wilson's disease is also very important for early detection of new cases.[8-9]

AIMS AND OBJECTIVES:

To study the spectrum of presentations in patients of Wilson's disease in Eastern India.

MATERIALS AND METHODS:

A cross-sectional study of ninety-nine (n=99) patients of Wilson's disease in Eastern India. This study was done in the Department of General Medicine, Rajendra Institute of Medical Sciences, Ranchi in collaboration with Advanced Diagnostic Centre, Ranchi.

INCLUSION CRITERIA:

Patients with-

(1) History and clinical examination suggestive of Wilson's disease.
(2) Presence of Keyser Fleischner (KF) ring by slit lamp examination.
(3) Decreased serum ceruloplasmin level (less than 20 mg/dl).
(4) Decreased serum copper level (less than 75µg/dl).

EXCLUSION CRITERIA:

Patients with extra-pyramidal symptoms but normal serum copper, normal serum ceruloplasmin and no Keyser Fleischner (KF) ring.

RESULTS:

Mean age at which patients presented to us was 14.32 years, with a range varying from eight to twenty-four years. The mean age of onset of illness in this study was found to be 11.81 years (range 6.5 to 23 years). Mean delay between the onset of symptoms and diagnosis of the illness was 2.24 years (range four months to six years). Majority of the patients in this study were male (M:F= 62:37).Presenting symptoms of the patients are tabulated below (Table 1):

Table 1: Presenting symptoms

Presenting symptoms	n(%)
Dysarthria	38(38.4)
Abnormal posturing of upper limbs	33(33.3)
Drooling of saliva	29((29.3)
Abnormal posturing of lower limbs	19(19.2)
Tremors	18(18.1)
Dysphagia	14(14.1)
Cognitive decline	12(12.1)
Unsteady gait	5(5)
Seizures	5(5)
Abnormal Behaviour	4(4)

On examination, dystonia and "Wilson facies with a characteristic grin" were the major clinical signs present in the patients under study. Of the ninety-nine patients, eighty one patients had dysarthria and sixty-nine patients showed cognitive decline on detailed examination.

The main clinical signs which were noted in the study are summarized in Table 2:

Table 2: Clinical signs

Clinical signs	n(%)
Dystonia	96(97)
Dystonic smile	95(96)
Dysarthria	81(81.8)
Cognitive decline	69(69.7)
Psychosis	48(48.5)
Tremors	46(46.5)
Bradykinesia	46(46.5)
Pyramidal signs	37((37.4)
Ataxia	28(28.3)
Seizures	18(18.2)
Myoclonus	4(4)

Positive family history was found in 44 cases (44.4%) and a study of family pedigree suggested autosomal recessive inheritance pattern. Among the unaffected siblings of twelve probands who could be screened for the illness, six of them showed abnormalities in the form of presence of Keyser Fleischer (KF) ring and low levels of serum copper and ceruloplasmin. All the screened patients were asymptomatic at the time of evaluation.

KF ring was seen on slit lamp examination in all but two patients (98%). Two patients in whom KF ring could not be detected showed severe biochemical abnormalities strongly suggestive of Wilson's disease.

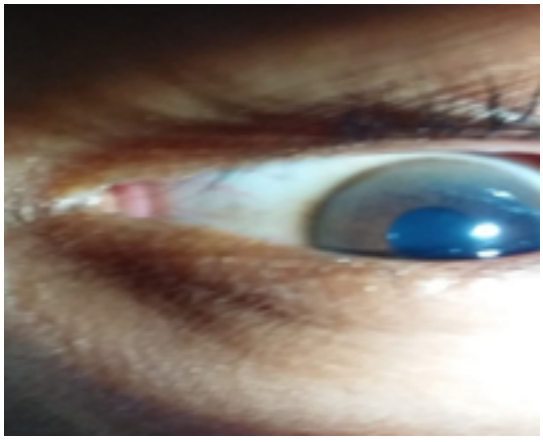

Figure 1: Kayser-Fleischer(KF) ring

Various biochemical findings in the patients are tabulated below(Table 3):

Table 3: Biochemical findings

Parameter	n(%)
Serum copper(<75µg//dl)	80(80)
Serum ceruloplasmin (<20mg/dl)	94(95)
24 hr urinary copper(>100µg)	99(100)

Neuroimaging could be done in 89 cases (CT in 60 and MRI in 29 cases). Basal ganglionic and thalamic changes could be seen in 27 cases (93%) on MRI and 38 cases (63%) on CT scan. White matter changes could be appreciated in 21 cases (72.4%) on MRI and 32 cases (53.3%) on CT scan. Brainstem changes could be seen in 18 cases (62%) on MRI and only 3 cases (5%) on CT scan .

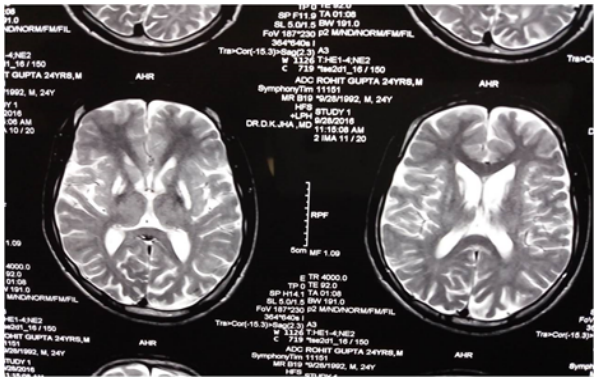

Figure 2: MRI Brain: T2W- hyper-intense areas in putamen & caudate bilaterally

DISCUSSION:

In this study, we found that the mean age of onset of symptoms of Wilson's disease in Eastern India was 11.81 years. The mean age of presentation was 14.32 years. Mean delay between the onset of symptoms and diagnosis of the illness was 2.24 years.

It was found that, in Eastern India, the major presenting complaints were dysarthria and abnormal posturing of upper limbs followed by drooling of saliva, abnormal posturing of lower limbs, tremor, dysphagia and cognitive decline in decreasing order of frequency. On examination, dystonia and characteristic Wilson facies was found in almost all the patients. Dysarthria and cognitive decline were also seen in a majority of cases. Psychosis, tremor and bradykinesia were also not very uncommon.

On slit lamp examination, KF ring was seen in almost all cases of symptomatic Wilson's disease.

Low levels of serum ceruloplasmin was found to be a more sensitive parameter for Wilson's disease than low serum copper. All symptomatic patients of Wilson's disease excreted >100µg of copper in urine over 24 hours.

MRI was found to be a more sensitive diagnostic tool than CT scan for evaluation of Wilson's disease. Basal ganglia and thalamic changes could be seen in majority of cases of Wilson's disease on MRI.

CONCLUSION:

Wilson's disease is an autosomal recessive disease with varied manifestations. In Eastern India, any child with slowly progressive extra-pyramidal symptoms must be evaluated for Wilson's disease. Low levels of serum copper, serum ceruloplasmin and increased urinary excretion of copper are very sensitive tests that may aid in diagnosing a case of Wilson's disease. MRI may also reveal characteristic changes in basal ganglia and thalamus in a majority of the patients.

ACKNOWLEDGEMENT:

(Late)Dr.K.K.Sinha, Ex-Director, Advanced Diagnostic Centre, Ranchi

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