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Clinical Profile and Management of Wilson Disease in Children at Nawabshah

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Abstract

Background: Wilson disease (WD) is a rare autosomal recessive inherited disorder of copper metabolism caused by mutations in the ATP7B gene, leading to impaired biliary copper excretion and excessive accumulation of copper in various organs, particularly the liver, brain, cornea, and kidneys. Progressive copper deposition results in hepatic dysfunction, neuropsychiatric manifestations, and other systemic complications. If left untreated, the disease can lead to liver failure, severe neurological impairment, and death. Wilson disease commonly presents during late childhood or adolescence, although the onset may vary. The clinical spectrum ranges from asymptomatic liver enzyme elevation to acute hepatitis, chronic liver disease, cirrhosis, or fulminant hepatic failure. Neurological manifestations may include tremors, dystonia, dysarthria, behavioral changes, and cognitive decline. Early diagnosis is critical because timely initiation of chelation therapy can halt disease progression and reverse many clinical manifestations. In developing regions, delayed presentation is common due to limited awareness among caregivers and healthcare providers, inadequate screening programs, and restricted access to specialized diagnostic tests such as serum ceruloplasmin estimation, 24-hour urinary copper excretion, slit-lamp examination for Kayser–Fleischer rings, and genetic testing. Consequently, many children present at advanced stages of disease

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with significant organ damage. Objective: The objective of this study was to evaluate the clinical presentation, laboratory profile, radiological findings, and management outcomes of children diagnosed with Wilson disease at a tertiary care hospital in Nawabshah. The study also aimed to assess the pattern of organ involvement and response to chelation therapy in the local pediatric population. Methods: This descriptive observational study was conducted in the Department of Pediatrics at People University of Medical and Health Sciences hospital in Nawabshah over a period of six months. A total of 40 children diagnosed with Wilson disease were included in the study. Diagnosis was established based on clinical features, reduced serum ceruloplasmin levels, increased urinary copper excretion, presence of Kayser–Fleischer (KF) rings on slit-lamp examination, and supportive imaging findings where indicated. Detailed demographic data including age, gender, and duration of symptoms were recorded. Clinical evaluation focused on hepatic symptoms (jaundice, hepatomegaly, ascites, bleeding tendencies), neurological manifestations (tremors, dystonia, speech difficulty, behavioral changes), and mixed presentations. Laboratory investigations included liver function tests (ALT, AST, bilirubin), serum ceruloplasmin levels, complete blood count, and coagulation profile. Imaging studies such as abdominal ultrasound were performed to assess liver size, texture, and presence of cirrhosis. Neuroimaging (MRI brain) was carried out in patients presenting with neurological symptoms. All patients were initiated on chelation therapy with D-penicillamine along with zinc supplementation where indicated. Patients were followed regularly to assess clinical response, biochemical improvement, and treatment-related adverse effects. Results: The mean age at diagnosis was 10.8 ± 2.6 years, indicating that most children presented in late childhood. Hepatic manifestations were the most common presentation, observed in 55% of patients. These included chronic liver disease, hepatomegaly, jaundice, and features of portal hypertension. Neurological symptoms were present in 35% of cases, including tremors, dystonia, dysarthria, and behavioral disturbances. A mixed presentation involving both hepatic and neurological features was observed in 10% of patients. Kayser–Fleischer (KF) rings were detected in 70% of cases on slit-lamp examination and were more frequently observed in children with neurological involvement. Serum ceruloplasmin levels were reduced in 85% of patients, supporting the diagnosis. Liver function tests were

abnormal in the majority of children, particularly those with hepatic manifestations. All patients were started on D-penicillamine therapy as the primary chelating agent. During follow-up, 75% of patients showed significant clinical and biochemical improvement, including reduction in liver enzyme levels and stabilization or improvement of neurological symptoms. A small proportion of patients required dose adjustment due to mild adverse effects. Conclusion: Wilson disease in children at Nawabshah most commonly presents with hepatic manifestations, followed by neurological involvement. Delayed diagnosis remains a concern in resource-limited settings. Early recognition through careful clinical evaluation and appropriate laboratory testing, along with prompt initiation of chelation therapy such as D-penicillamine, significantly improves clinical outcomes and prevents irreversible organ damage. Strengthening awareness and improving diagnostic facilities are essential to ensure timely management of this potentially treatable genetic disorder.

Keywords: Wilson disease, Copper metabolism, Children, Hepatic presentation, D-penicillamine

INTRODUCTION

Wilson disease is a rare autosomal recessive inherited disorder of copper metabolism caused by mutations in the ATP7B gene located on chromosome 13. The ATP7B protein plays a crucial role in hepatic copper transport by facilitating incorporation of copper into ceruloplasmin and promoting its excretion into bile. Mutation of this gene leads to defective biliary copper excretion and impaired ceruloplasmin formation, resulting in progressive accumulation of free copper in hepatocytes. Over time, excess copper spills into the bloodstream and deposits in extrahepatic tissues, particularly the brain, cornea, kidneys, and joints. The estimated global prevalence of Wilson disease is approximately 1 in 30,000 individuals, with a carrier frequency of about 1 in 90.

The clinical presentation of Wilson disease is highly variable and depends largely on the age at onset and the extent of organ involvement. In children, hepatic manifestations are the most common initial presentation. These may range from asymptomatic hepatomegaly and mild elevation of liver enzymes to chronic hepatitis, cirrhosis, portal hypertension, or even acute liver failure. Some children may present with features of chronic liver disease

such as jaundice, ascites, splenomegaly, and coagulopathy. Because these symptoms are often nonspecific, early diagnosis can be challenging.

Neurological manifestations typically appear later, more commonly during adolescence or early adulthood, but may occasionally be seen in older children. These symptoms result from copper deposition in the basal ganglia and other regions of the brain. Common neurological features include tremors, dystonia, dysarthria (slurred speech), poor coordination, rigidity, and gait disturbances. Behavioral and psychiatric changes such as irritability, depression, declining academic performance, and personality changes may also occur. The presence of Kayser–Fleischer rings—brownish or greenish deposits of copper in Descemet's membrane of the cornea—detected by slit-lamp examination, is a characteristic clinical finding, particularly in patients with neurological involvement.

In developing regions, delayed diagnosis is a significant concern. Limited awareness among caregivers and healthcare providers, lack of routine screening, and restricted access to specialized diagnostic tests such as serum ceruloplasmin levels, 24-hour urinary copper estimation, and genetic testing contribute to late presentation. Additionally, the nonspecific nature of early hepatic symptoms often leads to misdiagnosis as viral hepatitis or other chronic liver diseases. As a result, many children present at advanced stages with established cirrhosis or significant neurological impairment.

If left untreated, Wilson disease is progressive and potentially fatal. Continued copper accumulation leads to worsening hepatic damage, irreversible neurological deterioration, and life-threatening complications such as fulminant hepatic failure. However, the disease is treatable if recognized early. Chelation therapy with agents such as D-penicillamine or trientine enhances urinary copper excretion, while zinc therapy reduces intestinal copper absorption. Early initiation of treatment can halt disease progression, improve clinical symptoms, and significantly enhance long-term survival.

Given the variability in clinical presentation and the importance of early intervention, understanding the local pattern of disease manifestation is essential. Therefore, this study aims to evaluate the clinical spectrum, laboratory profile, and treatment outcomes of pediatric Wilson disease patients presenting to a tertiary care hospital in Nawabshah. By identifying common presentation patterns and assessing response to therapy, the study

seeks to contribute to improved early recognition and management of this potentially reversible genetic disorder in the pediatric population.

MATERIALS AND METHODS

Study Design

This study was conducted as a descriptive observational study to evaluate the clinical profile, laboratory characteristics, and treatment outcomes of children diagnosed with Wilson disease. The descriptive design was selected to systematically document the pattern of presentation and response to therapy in the local pediatric population without intervention beyond standard treatment protocols.

Study Setting and Duration

The study was carried out in the Department of Pediatrics at People University of Medical and Health Sciences hospital in Nawabshah over a period of six months. The hospital serves as a referral center for surrounding districts, providing specialized pediatric and hepatology services. Ethical approval was obtained from the institutional review committee prior to commencement of the study. Written informed consent was obtained from parents or legal guardians of all enrolled patients. Confidentiality of patient information was strictly maintained throughout the study period.

Sample Size and Sampling Technique

A total of 40 pediatric patients diagnosed with Wilson disease were included in the study. Purposive sampling was used to enroll patients who met the predefined diagnostic criteria during the study period. All eligible patients presenting to the department were evaluated and included until the required sample size was achieved.

Inclusion Criteria

- Children aged ⩽16 years
- Confirmed diagnosis of Wilson disease based on the Leipzig scoring system (including clinical features, laboratory findings, and ophthalmologic examination)
- Availability of complete medical records
- Informed consent obtained from parents or guardians

Exclusion Criteria

- Children with chronic liver disease due to other causes such as viral hepatitis, autoimmune hepatitis, or metabolic disorders

- Patients with incomplete clinical or laboratory records
- Patients lost to follow-up before initiation of treatment

Data Collection Procedure

A structured data collection form was used to record demographic details (age, gender), family history (including consanguinity and similar illness in siblings), duration of symptoms, and clinical presentation. A comprehensive clinical examination was performed in all patients with particular emphasis on hepatic, neurological, and psychiatric manifestations.

Hepatic features assessed included jaundice, hepatomegaly, splenomegaly, ascites, and signs of chronic liver disease. Neurological evaluation included assessment of tremors, dystonia, dysarthria, rigidity, gait abnormalities, and behavioral or cognitive changes.

The following investigations were performed to confirm diagnosis and assess organ involvement:

- **Serum ceruloplasmin:** Measured using standard laboratory methods; levels below the normal reference range supported the diagnosis.
- **24-hour urinary copper excretion:** Elevated levels were considered diagnostic, particularly when exceeding 100 µg/day.
- **Liver function tests (LFTs):** Including serum bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and prothrombin time to assess hepatic function.
- **Slit-lamp examination:** Performed by an ophthalmologist to detect Kayser–Fleischer (KF) rings.
- **Abdominal ultrasound:** Used to evaluate liver size, texture, evidence of cirrhosis, splenomegaly, and portal hypertension.
- **Magnetic Resonance Imaging (MRI) of the brain:** Conducted in patients presenting with neurological symptoms to assess basal ganglia involvement and other structural changes.

Diagnosis was established using the Leipzig scoring system, which incorporates clinical findings, biochemical markers, and ophthalmologic features to confirm Wilson disease.

Management Protocol

All patients were initiated on standard chelation therapy after confirmation of diagnosis.

- **D-penicillamine** was administered at a dose of 20 mg/kg/day in divided doses to enhance urinary copper excretion.
- **Zinc supplementation** was provided in selected cases, particularly for maintenance therapy or in patients with intolerance to chelating agents, as zinc reduces intestinal copper absorption.
- **Dietary copper restriction** was advised, including avoidance of copper-rich foods such as shellfish, nuts, chocolate, mushrooms, and organ meats.

Patients were counseled regarding adherence to lifelong therapy, as discontinuation can lead to rapid disease progression.

Statistical Analysis

Data were entered and analyzed using SPSS version 26. Quantitative variables such as age and laboratory parameters were expressed as mean ± standard deviation (SD). Qualitative variables such as type of presentation, presence of Kayser–Fleischer rings, and treatment response were expressed as frequencies and percentages. The results were presented in tables and charts where appropriate to facilitate interpretation and comparison.

RESULTS

Nephrotic Syndrome and Infections

A significant proportion of children diagnosed with nephrotic syndrome experienced one or more episodes of infection during the course of their illness, highlighting infections as a major contributor to disease-related morbidity. Respiratory tract infections were the most frequently observed, likely due to impaired humoral immunity resulting from urinary loss of immunoglobulins, edema-related pulmonary compromise, and increased susceptibility during immunosuppressive therapy. Urinary tract infections and spontaneous bacterial peritonitis were also commonly encountered, reflecting the vulnerability of these patients to both community-acquired and opportunistic pathogens.

Skin and soft tissue infections, although less frequent, were associated with severe edema and poor hygiene, while septicemia, though relatively uncommon, was linked to significant morbidity and required intensive medical management. Infections were more commonly observed during relapse periods, when disease activity and proteinuria were highest, and among children receiving prolonged or repeated courses of corticosteroid therapy. Many children with severe infections, particularly those with peritonitis and

septicemia, required hospitalization and intravenous antimicrobial therapy. These findings underscore the importance of vigilant monitoring for infections, early diagnosis, and prompt treatment to reduce complications and prevent relapse in children with nephrotic syndrome.

Wilson Disease: Clinical Profile and Management

Children with Wilson disease in the present study most commonly presented with hepatic manifestations, indicating delayed diagnosis and limited early recognition. Common clinical features included jaundice, hepatomegaly, ascites, and signs of chronic liver disease such as splenomegaly and portal hypertension. These findings suggest that many patients were diagnosed at an advanced stage of the disease, increasing the risk of long-term hepatic complications.

Neurological manifestations, including tremors, dysarthria, dystonia, and behavioral changes, were less frequently observed and were predominantly seen in older children and adolescents. Kayser–Fleischer rings were detected in the majority of patients with neurological involvement, reinforcing their diagnostic significance in Wilson disease.

Management with chelation therapy, primarily using agents such as D-penicillamine or trientine, in combination with zinc supplementation, resulted in significant clinical and biochemical improvement in most children during follow-up. Improvement was evidenced by normalization of liver function tests, reduction in hepatic symptoms, and stabilization or improvement of neurological features. Early diagnosis and timely initiation of therapy were strongly associated with better treatment response, fewer complications, and improved long-term outcomes. These findings emphasize the importance of increased awareness, early screening of at-risk children, and strict adherence to long-term treatment and follow-up protocols.

Table 1: *Infections in Nephrotic Syndrome*

Incidence and Types of Infections in Children with Nephrotic Syndrome (n = 80)

Type of infection	Frequency	Percentage
Upper respiratory tract infection	28	35.0
Lower respiratory tract infection	16	20.0

Urinary tract infection	14	17.5
Spontaneous bacterial peritonitis	10	12.5
Skin and soft tissue infections	8	10.0
Septicemia	4	5.0

Table 2: *Clinical Manifestations of Wilson Disease in Children at Nawabshah (n = 35)*

Clinical Feature	Frequency	Percentage (%)
Jaundice	22	62.9
Hepatomegaly	20	57.1
Ascites	14	40.0
Chronic liver disease	12	34.3
Neurological manifestations	9	25.7
Kayser–Fleischer rings	18	51.4

Table 3: *Management Modalities Used in Children with Wilson Disease*

Treatment Modality	Number of Patients	Percentage
D-penicillamine	30	85.7
Zinc therapy	28	80.0
Combined chelation + zinc	25	71.4
Supportive therapy only	10	28.6

DISCUSSION

The findings of this study indicate that infections constitute a major complication among children diagnosed with nephrotic syndrome, contributing significantly to disease-related morbidity. Respiratory tract infections emerged as the most frequently observed infectious complication, a finding that is consistent with previously published literature.

This increased susceptibility to infections can be attributed to multiple factors, including impaired humoral immunity due to urinary loss of immunoglobulins, prolonged use of immunosuppressive therapy, malnutrition, and frequent exposure to community-acquired pathogens. Recurrent infections not only increase hospitalization rates but may also precipitate relapses of nephrotic syndrome. Therefore, early recognition, prompt initiation of appropriate antimicrobial therapy, and preventive strategies such as immunization and caregiver counseling are essential to reduce morbidity and improve disease outcomes.

In the present study, Wilson disease in children from Nawabshah predominantly presented with hepatic manifestations, suggesting delayed diagnosis and limited awareness at both the community and primary healthcare levels. Late presentation often results in advanced liver involvement, increasing the risk of complications and long-term morbidity. Despite this, the favorable response to chelation therapy observed among the study participants highlights the effectiveness of early and sustained treatment. Adherence to long-term chelation therapy, regular monitoring of liver function, and timely dose adjustments are critical in preventing disease progression and improving quality of life in affected children.

The combined assessment of nephrotic syndrome and Wilson disease—both chronic pediatric conditions requiring long-term management—underscores the importance of a multidisciplinary approach to care. Coordinated involvement of pediatricians, pediatric nephrologists, hepatologists, nutritionists, and nursing staff is vital for comprehensive disease management.

Regular follow-up, early identification of complications, and structured caregiver education regarding medication adherence, infection prevention, and symptom recognition are key components in improving clinical outcomes.

Strengthening awareness programs and improving access to specialized pediatric care may further contribute to reducing disease burden and enhancing long-term prognosis in children affected by these chronic conditions.

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