

**Case Study**

**A CASE REPORT ON WILSON'S DISEASE: A RARE CLINICAL CONDITION OF COPPER DEPOSITION IN LIVER**

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**ABSTRACT**

Wilson's disease is a rare inherited disorder and is characterized by the accumulation of copper in various tissues and also in organs like the liver, brain, kidneys and cornea. Symptoms in paediatrics characteristically appear with hepatic involvement. In this case we have discussed about an eleven-year-old male child, who was presented to the Paediatric department in a tertiary care hospital with chief complaints of yellowish discoloration of eyes, dark coloured urine and high grade fever. Due to the accumulation of copper there were decreased levels of ceruloplasmin and there was an increased 24 hour urinary copper, which confirms the Wilson's disease in this child. Child was treated with Cephalosporin antibiotics, vitamins, laxative, and bile acid sequestrants. Child showed gradual improvement in clinical symptoms and got discharged without any further event. Quality of evidence was assessed according to the GRADE system. Early diagnosis and management helped to prevent serious complications.

**Keywords:** Paediatric, Ceruloplasmin, Copper, Wilson's disease

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**INTRODUCTION**

Wilson Disease (WD) is an intermittent autosomal receding disease subsequent in a systemic excess of copper. The stated incidence is 30 per million people [1]. Wilson's disease occurs due to mutations of the ATP7B gene on chromosome 13, which encodes a copper-transporting P-type ATPase (ATP7B) that exists in the trans-golgi complex of hepatocytes. ATP7B is mainly liable for entrapping copper from intracellular chaperone proteins into the secretory pathway, for the both excretion into bile and also for the integration into apo-ceruloplasmin for the synthesis of functional ceruloplasmin. Wilson's disease develops due to the build-up of copper in affected tissues [2]. Copper is a crucial contented of many metabolic enzymes. Usual predictable total body copper is 50-100 mg and average daily intake of copper is 2-5 mg. The amount of copper in the body is average during birth. Afterwards, it increases progressively. Generally, the symptoms initiate between the ages 5 and 45 y [3]. The main complications of Wilson's disease include brain damage and liver cirrhosis, psychiatric disturbances, i.e., depression, suicidal tendencies, and aggressive behaviour motor dysfunction and corneal opacities [4]. The simple diagnostic method comprises serum ceruloplasmin and 24hour urinary copper excretion. Final diagnosis of Wilson disease can be recognized using a diagnostic scoring system based on symptoms, biochemical tests which assess copper metabolism and molecular analysis of mutations in the ATP7B gene. The Grades of Recommendation, Assessment, Development and Evaluation (GRADE) system of diagnosis is described below.

**GRADE system as used European association for the study of the liver (EASL) clinical practice guidelines (159)**

High-Quality Further research is very unlikely to change our confidence in the estimated effect.

Moderate Quality Further research is likely to have an important impact on our confidence in the estimate effect and may change the estimate.

Low Quality Further research is likely to have an important impact on our confidence in the estimate effect and is likely to change the estimate is uncertain.

**Recommendation**

Strong-Factors influencing the strength of recommendation included the quality of evidence, presumed patient-important outcomes and costs.

Weak-Variability in preferences and values, or more certainty, higher costs or resource consumption.

**System of recommendation as used in the American Association for the study of liver disease (AASLD) practice guidelines (130)**

Class I-Conditions for which there is evidence and general agreement that a given procedure or treatment is beneficial, useful and effective.

Class II-Conditions for which there is conflicting and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.

Class IIa-Weight of evidence/opinion is in favour of usefulness/efficacy.

Class IIb-Usefulness/efficacy is less well established.

**Level of evidence**

Level A-Data derived from multiple randomized clinical trials or meta-analyses

Level B-Data derived from a single randomized trial, or nonrandomized studies.

Level C-Only consensus opinion of experts, case studies.

Here we discussed about a case of Wilsons disease, which was diagnosed on an 11 y old male child with ceruloplasmin and 24hr urinary copper levels.

**Case presentation**

An 11yrs old male child was presented in a tertiary care hospital on 27/11/2019 with chief complaints of (C/O) yellowish discoloration of eyes, passing of yellow coloured urine since last two months, high grade continuous acute onset of fever since 4 d with no relief by medication. Fever was not associated with chills and sweating. Complaint of itching sensation since 4 d was also noted. On clinical examination (O/E) his vitals were found to be stable with a slight increase of temperature (100 ° F). The past history of the patient revealed that he was passing yellow coloured urine since past two months and discoloration of eyes. History of patient's present illness indicated icterus positive, which enumerate conjugated jaundice. His past medical history discloses decreased appetite and he was on Tab. Cefixime, Syp. Liv-52 and Syp. Lactulose since one month. He was treated with Syp. Folic acid, Syp. Paracetamol 250

and Syp. Multivitamin for 10 d after consultation with another doctor. Then the family consulted a local registered medical practitioner and he was given herbal medication once in a week for 3 w, which was to be mixed in curd and taken. He developed itching and it got subsided by itself.

Upon admission child was prescribed with:

Rx

1. Inj. Hepatic drip 100 ml in 400 ml NS
2. IVF. Dextrose 10%
3. Inj. Potassium chloride 5 ml, Calcium Gluconate 5 ml and multi Vitamin 2 ml @ 70 ml/h

4. Inj. Vitamin K 5 mg IV OD
5. Inj. Cefotaxime 1.5 gm IV BID
6. Inj. Ranitidine 50 mg IV BID
7. Syp. Lactulose 7 ml PO QID
8. Tab. Ursodeoxycholic acid 50 mg PO TID
9. Cap. Vitamin A and D PO Once in a Week
10. Cap. Vitamin E PO OD
11. Lab findings:

His lab report findings are described in table 1.

**Table 1: Parameters with observed values and normal range**

Complete blood picture (28/11/19)	Observed values	Normal range
Haemoglobin	10.8	12-15 mg/dl
RBC	3.93	3.8-4.8 mln/cumm
WBC	8.40	4-11 Th. cells/cumm
Platelets	392	150-400L/cumm
Neutrophils	03	40-80%
Lymphocytes	4.15	20-40%
Monocytes	0.58	2-10%
Eosinophils	0.64	0-6%
Basophils	0.01	0-2%
Serum Electrolytes (28/11/19)	Observed values	Normal range
Sodium	138	135-150mEq/l
Potassium	4.2	3.5-5mEq//l
Chloride	102	96-106mEq/l
Renal function test and Liver function test (28/11/19)	Observed values	Normal range
Total Serum Bilirubin	3.81*	0.2-1 mg%
SGPT	198.6*	7-56U/l
Alkaline Phosphate	95.9	42-362U/l
Serum Creatinine	0.35*	0.6-1.2 mg/dl
Blood Urea	10.13*	15-40 mg/dl
APTT	30.3	30-40 Se
Prothrombin Time	14.0*	11.0-12.5 Sec
International Normalized Ratio	1.17	0.9-1.1 sec
Ceruloplasmin (30/12/19)	08**	20-35 mg/dl
24h Urinary Copper (30/11/19)	293**	20-50µg
Note: *-Indicates abnormal values (higher or lower than normal values)		
** -Indicates highly abnormal values (confirmatory diagnostic values)		
Ultrasound (3/11/19)	Impression: Grade-I Fatty infiltration of the liver	
Genetic Analysis (2/12/19)	Genetic analysis was found to be negative for Wilson's disease.	

**Table 2: Conformational diagnosis describes about the diagnosis**

Tests	Values observed	Normal value
24hr Urinary Copper	293	20-50µg
S. Ceruloplasmin	08	20-35 mg/dl

With various lab tests and other assessment criteria, the patient was diagnosed as Wilson's disease and his prescription throughout the admission period are explained below.

### Treatment

#### Day-2 (28/11/19)

1. IVF Hepatic drip 70 ml/hr
2. Inj. Vitamin K 5 mg IV STAT
3. Syp. Lactulose 7 ml P/O QID
4. Tab. Ursodeoxycholic acid 150 mg P/O TID
5. Vitamin A and D 1 tab P/O OD
6. Vitamin E 1 tab P/O OD
7. Inj. Cefotaxime 1.5 gm IV BID
8. Inj. Ranitidine 50 mg IV BID

He was referred to an ophthalmologist and diagnosed as papillar positive; evidence of Kayser-Fleischer ring (fig. 1)



**Fig. 1: Image of kayser-fleischer ring**

**Day-3 (29/11/19)**

He was referred to the pathologist to do hemograph with red count and haemoglobin levels were slightly less (10.8 gm/dl) and continued the same treatment.

**Day-4 (30/11/19)**

Continued the same treatment and advised for 24hr urinary copper test.

**Day-5 (1/12/19)**

There were no fresh complaints and IVF hepatic drip was stopped.

**Day-6 (2/12/19)**

The child was active and the same treatment was given and Inj. Cefotaxime was stopped.

**Day-7 (3/12/19)**

Same treatment was continued

**Day-8 (4/11/19)**

Same treatment was continued and 24hr urinary copper level was found to be 16.5 µg/h.

**On Day-9 (5/12/19)**

Patient was found to fit to discharge and Kayser-Fleischer ring in eyes was completely diminished (fig.2) with the following discharge medicine and advised to come for review after 2 w.



**Fig. 2: Image after child recovery**

Discharge medication:

Rx

Tab. Ursodeoxycholic acid 150 mg PO BD

Tab. B complex PO OD

Vitamin A and D PO OD

Vitamin E PO OD

**DISCUSSION**

Here we present the Case study of an 11 y old child with Wilson's disease. The patient's past history and present history upon admission was evaluated clinically and Provisional and Confirmational diagnosis enumerated. Clinical lab findings were a guide to start therapeutic regimen and patient improved with time. Here we present our role as a Clinical Pharmacist in evaluating the Case further with established standard guidelines. Table 5 and table 6 depict the Ferenci Score and diagnostic approach of the Case.

**Table 3: Stepwise approach to diagnose Wilson's disease**

Diagnostic approach to Wilson's Disease		
1. Clinical evaluation for Hepatosplenomegaly, ascites, K-F ring.	Molecular testing	Liver copper
2. Liver tests-ALT/AST, Bilirubin total/direct, INR.	(Common mutations, whole gene sequencing)	(If molecular testing inconclusive or not available)
3. Biochemical tests of copper metabolism-serum ceruloplasmin, 24h urinary copper.		

**Table 4: Diagnostic score in Wilson's disease**

Score	-1	0	1
Kayser-Fleischer rings	-	-	Present
Neuropsychiatric symptoms	-	Absent	-
Liver copper quantitative	Normal	-	-
Urinary copper	-	-	Present
Serum Ceruloplasmin	-	-	Present

**Table 5: Represent diagnostic score of Wilson's disease**

0-1 Unlikely	2-3 Probable	4 or more highly likely
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Our assessment shows a score of 2-3 showing an outcome of Probable. Additionally, Quality of evidence was assessed according to the GRADE system which enumerated the following parameters viz., Evidence: -Moderate quality, Recommendation-Strong, Classification-Class IIa, Level of Evidence-Level C. Patient's health condition improved with the therapeutic intervention.

Maintenance of proper diet *al.* so plays a vital role along with treatment. Generally, the patient was advised to avoid eating foods containing high copper amounts, such as chocolate, nuts, mushrooms, legumes and shellfish (lobster) and avoid drinking water from atypical sources like well water and instead it should be replaced with purified water. Early diagnosis and treatment helped in reducing symptoms. The patient's condition improved and vitals were normal. The urinary copper level came to normal. Proper medication care, low copper diet should be taken in order to show a reduction in mortality

**CONCLUSION**

Based on this Case study and our findings we conclude that, even though the case was treated appropriately and discharged accordingly, a further recommendation of an extensive investigation of all clinical parameters would be more appropriate in order to establish a strong Quality of evidence by the GRADE system. This would empower Clinicians to establish research findings correlating Clinical evidence with outcomes.

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**ABBREVIATIONS**

GRADE- The grades of recommendation, assessment, development and evaluation, EASL- European association for the study of the liver, AASLD- The American association for the study of liver disease, Syp- Syrup, Tab - Tablet, IVF- Intravenous fluids, NS- Normal Saline, Hr- Hour, ml- Millilitre, PO- Per Oral, Cap- Capsule, RBC- Red Blood Cells, WBC- White Blood Cells, APTT- Activated Partial Thromboplastin Time, SGPT- Serum Glutamic Pyruvic Transaminase, ALT- Alanine Transaminase, AST- Aspartate Aminotransferase, INR- International Normalized Ratio, STAT- Single Dose.

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**AUTHORS CONTRIBUTIONS**

All the authors have contributed equally.

**CONFLICT OF INTERESTS**

Declared none

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