CLINICAL APPROACH IN WILSON DISEASE USING LEIPZIG SCORING SYSTEM

D. Gancheva, M. Atanassova, M. Stamboliyska, I. Kotzev, M. Kaneva*

Clinic of Hepatogastroenterology
University hospital "St. Marina", Varna, Bulgaria
Department of Statistics*, University of Economics, Varna, Bulgaria

INTRODUCTION

Wilson disease (WD) is an autosomal recessively inherited disorder of the copper accumulation and toxicity. It's treatable, if diagnosed early. The recognition is clear in typical clinical presentations. Unexplained liver tests abnormalities are a diagnostic challenge and require more examinations.

AIM

To investigate the clinical features and diagnostic possibilities in WD, using Leipzig scoring system.

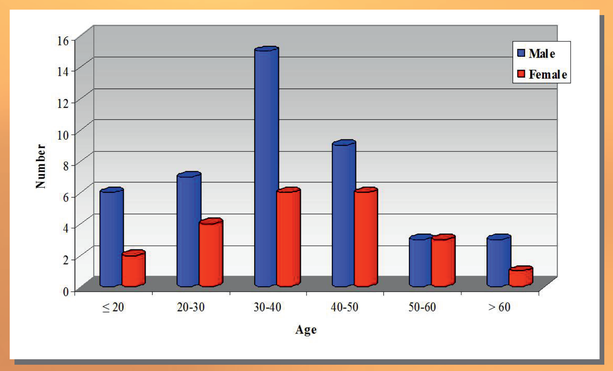
PATIENTS

- Clinical data and laboratory parameters were analysed in 65 patients with Wilson disease - 43 male, 22 female, mean age 37,75±12,98 (18 – 65).
- Control group – 17 patients with chronic liver diseases (CLD) – nonalcoholic steatohepatitis, autoimmune hepatitis, liver cirrhosis.

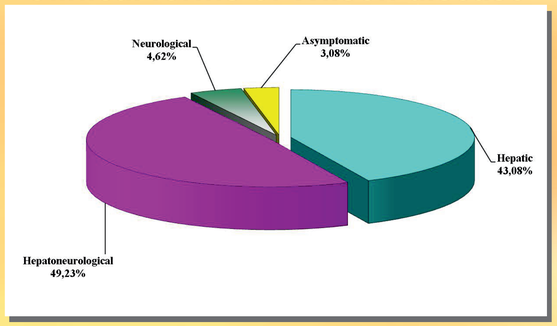
METHODS

- Medical history
- Physical and neurological examination
- Serum ceruloplasmin
- Urinary copper excretion
- Abdominal ultrasonography
- Liver biopsy
- Ophthalmological examination
- MRI of the brain
- DNA analysis
- Leipzig scoring system
- Statistical methods – descriptive statistics, empirical distribution, Student's t-test

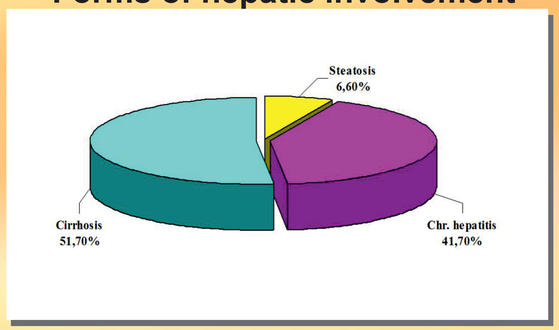
Age of the patients with Wilson disease



Clinical forms of Wilson disease



Forms of hepatic involvement

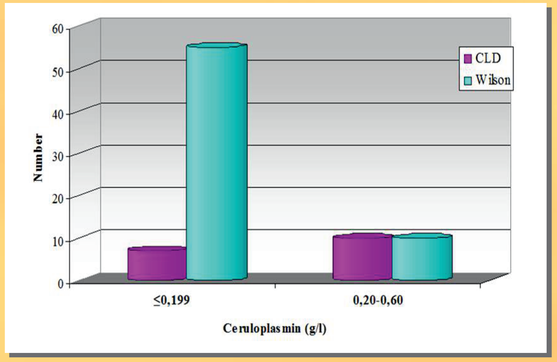


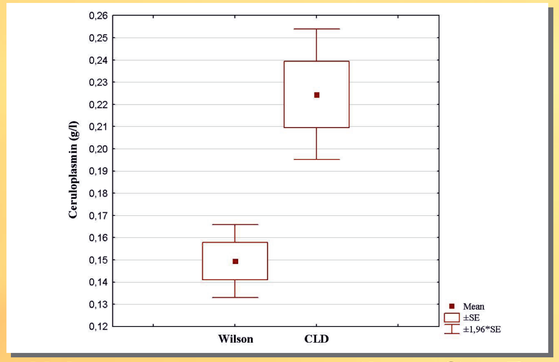
Co-exsisting diseases

Disease	*n*	*Gender*	*Treatment*
Hepatocellular carcinoma on liver cirrhosis	1	m	Sorafenib Ramucirumab
Chronic hepatitis B	1	m	Tenofovir
Chronic hepatitis B	1	m	Telbivudine
Hepatitis B liver cirrhosis	1 1 1	m m m	Lamivudine Not treated Not treated
Chronic hepatitis C	1	m	Peg IFN+Ribavirin
Autoimmune hepatitis	1 1	m f	Budesonide, UDCA UDCA
Primary biliary cirrhosis	1	m	Budesonide UDCA
Cholelithiasis	10	6f, 4m	
Dyslipidaemia	24	5f, 19m	Statins Fibrates

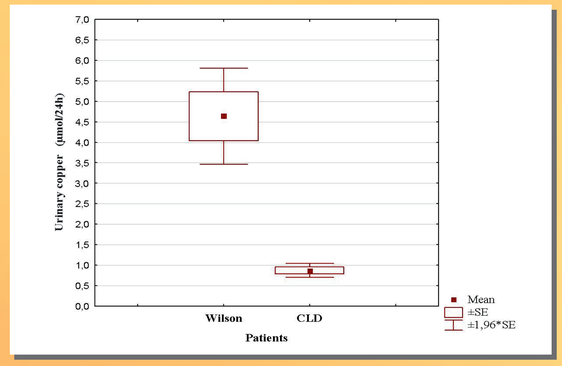
RESULTS

Serum ceruloplasmin

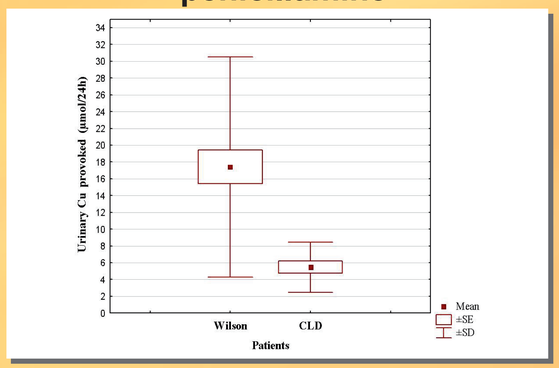




Basal urinary copper excretion



Urinary copper excretion after D-penicillamine



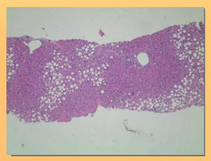
Histological findings

<u>Liver biopsy – 23/65</u>

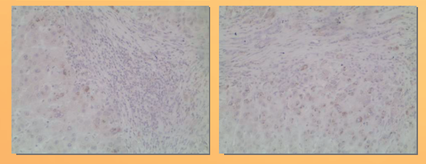
- Steatosis – 15
- Fibrosis – 11
- Glycogen-containing nuclei – 11
- Inflammatory infiltration – 11
- Necrosis – 5
- Pseudolobules – 2
- Regenerative nodules – 2
- Mallory's bodies - 2

<u>Rhodanine staining – 19/23</u>

- Positive – 10/19



Fibrosis and fatty degeneration
HE stain, x 200



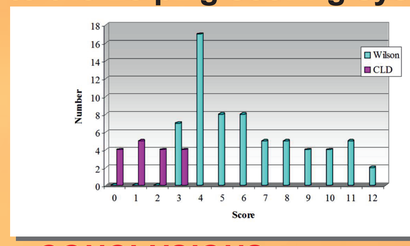
Copper deposits
Rhodanine stain, x 200

Clinical findings according to the Leipzig diagnostic criteria

Typical clinical findings	*n*	*Other tests*	*n*
KF rings	23/64	Liver biopsy	23/65
Sunflower cataract	5/64	Rhodanine-positive staining	10/19
Neurologic symptoms	35/65	Urinary copper	
		normal	10/65
		>2x ULN	37/62
Abnormalities at brain MRI	15/25	after D-penicillamine:	
		> 5x ULN	38/43
		> 10x ULN	32/43
Serum ceruloplasmin <0,2 g/l	55/65	Mutations detected	26/54
Coombs-negative hemolytic anemia	7/65		

KF – Kayser – Fleischer, MRI – magnetic resonance imaging
ULN – upper limit of normal

Distribution of the patients according to the Leipzig scoring system



CONCLUSIONS

- Wilson disease has to be considered in unexplained liver disease, hemolysis and neurological symptoms.
- The levels of the serum ceruloplasmin are significantly lower in our patients and can be used in the diagnosis of WD.
- Basal and D-penicillamine stimulated urinary copper excretion show significant elevation in WD patients and are useful non-invasive diagnostic test.
- The most common histological findings in our patients are not specific, but may suggest or confirm WD and are helpful for diagnosis.
- The Leipzig scoring system with the combination of clinical symptoms, laboratory parameters of copper metabolism, genetic testing and liver biopsy is reliable method for diagnosing of Wilson disease in clinical practice.