Berkshire and Surrey Pathology Services

Black Country Pathology Services

A National Audit on Wilson Disease

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Introduction:

Wilson Disease is a rare autosomal recessive disorder of copper metabolism, caused by a defect in the gene encoding the ATP7B transporter. Copper accumulation in the liver, brain and other organs can lead to hepatic, neurological and psychiatric manifestations.

Audit Aims and Method:

The audit aimed to capture current clinical and laboratory practice around screening for, diagnosing, and monitoring treatment of Wilson Disease. A questionnaire was distributed to LabMed members *via* Survey Monkey. Findings were critically assessed against British Association for the Study of the Liver (BASL, 2022), European Association for the Study of the Liver (EASL, 2012) and American Association for the Study of Liver Diseases (AASLD, 2022) guidance.

Results:

There were 52 respondents representing secondary care and paediatric hospitals, and specialist Wilson Disease centres.

Clinical protocols for Wilson Disease

Only 36% (*n*=18) of respondents had a clinical protocol for Wilson Disease, commonly as part of a liver protocol (*n*=11) with no neurology or laboratory involvement. Exclusion of Wilson Disease using age featured in nine (50%) protocols. Family screening (*n*=14, 78%) and recognition of non-immune haemolytic anaemia as a possible disease manifestation (*n*=11, 61%) were variably covered. Eleven sites used the Leipzig diagnostic scoring system.

Assessing suspected Wilson Disease

From Figure 1, routinely performed tests included caeruloplasmin, serum copper, 24h-urine copper excretion and haemolysis markers. Tests occasionally performed included, D-penicillamine challenge tests and random urine copper, whilst copper-65 absorption and calculated non-caeruloplasmin bound copper were rarely used.

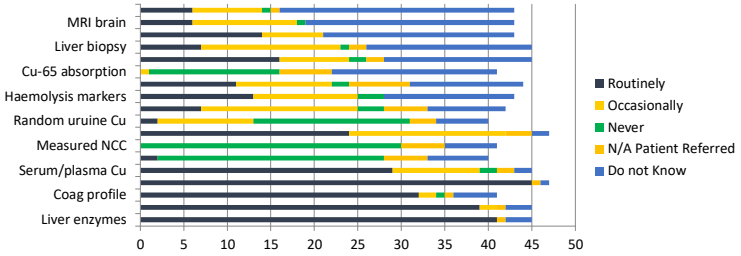

Figure 1. Tests advised / performed in assessing suspected Wilson Disease

Use of diagnostic tests

Most respondents used D-penicillamine challenge tests in paediatrics and/or when basal 24h urine copper was inconclusive, although nine indicated use in adults (Figure 2a). A minority (*n*=2) measured liver copper in all cases of suspected or diagnosed Wilson Disease (Figure 2b) Genetic testing for ATP7B mutations was used in accordance with guidance but it was unclear as to whether it was routinely performed prior to, or following, liver biopsy (Figure 2c)

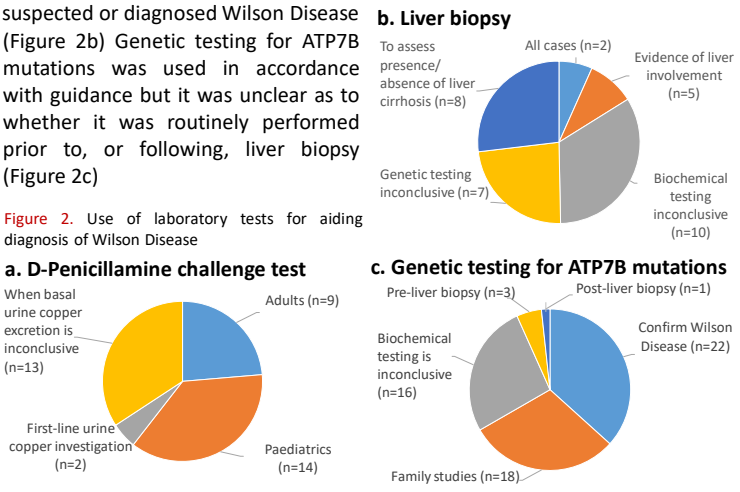

Figure 2. Use of laboratory tests for aiding diagnosis of Wilson Disease

Diagnostic thresholds

Diagnostic cut-off values provided for caeruloplasmin and 24h urine copper were wide-ranging (Figure 3), reflecting use of difference guidance, as well as at times being inconsistent with any guidance.

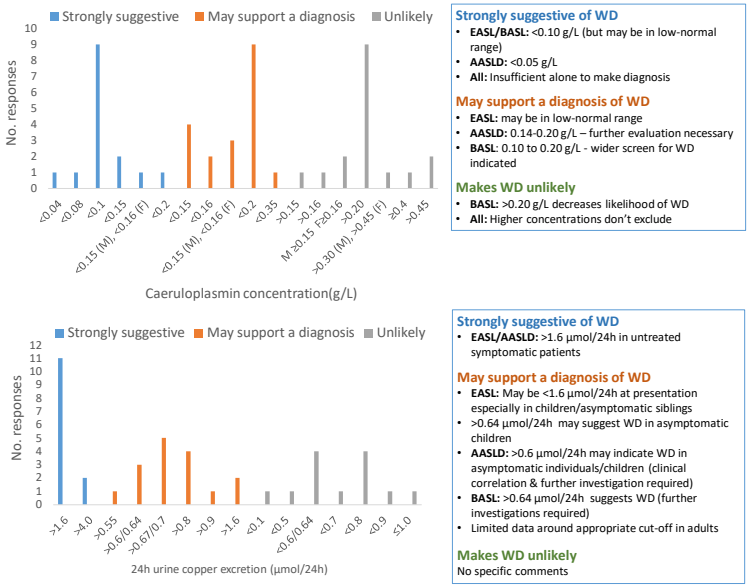

Figure 3. Diagnostic thresholds for caeruloplasmin (top) and 24h-urine copper (bottom)

Monitoring treatment for Wilson Disease

From Figure 4, routine tests for treatment monitoring included caeruloplasmin, serum copper and 24h-urine copper. Few or no sites used urine zinc excretion, random urine copper, or calculated non-caeruloplasmin bound copper.

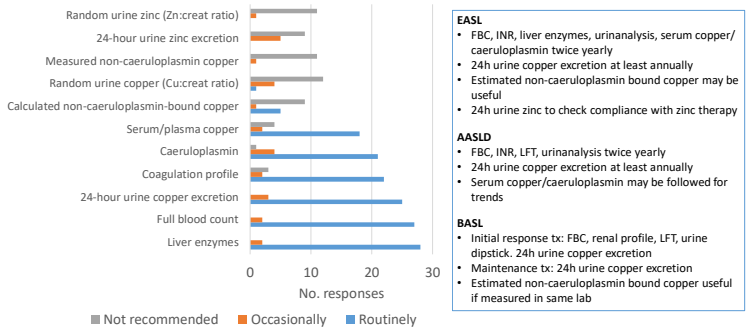

Figure 4. Tests advised / performed in assessing suspected Wison Disease

A wide range of 24h-urine copper treatment monitoring thresholds were provided by respondents (Figure 5).

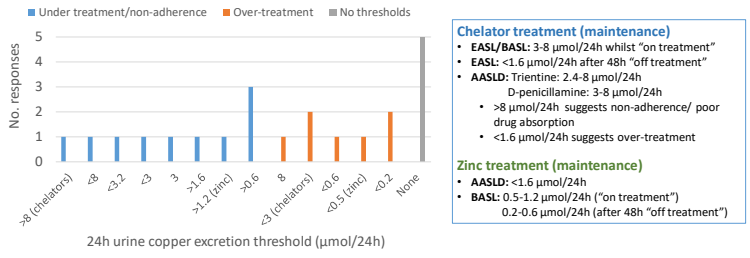

Figure 5. 24h-urine copper treatment monitoring thresholds

Conclusions:

A standardised UK approach is required to reduce variation in practice, *e.g.*, to use of D-penicillamine challenge tests and diagnostic thresholds. Practice contrary to all guidance needs to be addressed, *e.g.*, excluding Wilson Disease based on age, D-penicillamine challenge tests in adults, random urine copper for diagnosis, and over-requesting of serum copper.