Lay Language Summary of the Article “Liver involvement in congenital disorders of glycosylation (CDG). A systematic review of the literature”

What does the liver do? How is that affected by sugars (glycans)?

The liver is like a factory that transforms the food we eat into fuel (energy) and building materials that our cells can use to grow and work as needed. At the same time the liver is also working to eliminate the part of the food we ingested that is not necessary or that is toxic. The liver is also responsible for the production of chemicals that will be used in food digestion (bile fluid or bile juices).

Other (less known) roles:

- Prevent infections;
- Make proteins that help coagulation (coagulation is the process that makes your blood clot when it needs to, e.g. when a vessel is torn or cut, after a wound);
- Store vitamins, minerals, fats and sugars for your body to use when necessary (e.g. when you’re fasting).

Actually, the liver is a major site of glycosylation (of attachment of sugars to proteins/fats) in the body. It produces most of the glycosylated serum (blood component) proteins.

Defects in the process and machinery responsible for attaching sugars to proteins/fats can be expected to affect liver development, structure, and function.

How and to what extent were analysed and discussed in this scientific revision of literature.

Propose title for the lay summary:

**Liver disease in congenital disorders of glycosylation (CDG)**

You can access the article’s abstracts [HERE](#).

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You can access a “community-friendly” resource on liver affectation in CDG [HERE](#).
Take home messages

- At least 12% of all CDG forms have liver affectionation;
- Liver symptoms and signs include increased levels of transaminases (proteins produced in the liver whose increased levels are usually indicative of liver dysfunction), hepatomegaly (enlarged liver), liver steatosis (fatty liver), liver fibrosis (liver tissue is replaced by fibrotic tissue), liver cirrhosis and decreased antithrombin (a protein produced in the liver and responsible for stopping the coagulation process) levels;
- Liver failure can also occur in CDG patients. In contrast with liver cirrhosis – which is a chronic, slow evolving process that leads to the liver to stop working – liver failure is a rapid, sudden complete malfunction of the liver;
- Liver disease has been reported to lead to premature death in CDG patients. However, if timely diagnosed and closely monitored, liver disease can be effectively managed and treated;
- Hepatologists (clinicians specialised in liver diseases) are still widely unaware of CDG and still do not frequently recognise CDG as a cause of liver disease;
- Liver transplant has been successfully performed in CDG patients, being currently an approved therapy in Europe for MPI-CDG, ATP6VAP1-CDG and CCDC115-CDG patients;
- Liver diseases are probably underestimated in CDG;
- CDG should be tested in patients without a diagnosis and presenting with liver manifestations shown by CDG patients, especially when other probable diagnosis for liver disease have been excluded.

Table 1- CDG with major and minor liver affectionation

<table>
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<tr>
<th>CDG with major liver affectionation</th>
<th>CDG with minor liver affectionation</th>
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<tbody>
<tr>
<td>MPI-CDG, TMEM199-CDG, CCDC115-CDG, ATP6AP1-CDG</td>
<td>PMM2-CDG, ALG1-CDG, ALG3-CDG, ALG6-CDG, ALG8-CDG, ALG9-CDG, PGM1-CDG, COG1-CDG, COG4-CDG, COG5-CDG, COG6-CDG, COG7-CDG.</td>
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Main signs & symptoms

CDG with major liver affectionation

**MPI-CDG:** Enlarged liver, coagulopathy (defects in the blood coagulation mechanism), elevated transaminases, liver fibrosis and fatty liver.

**TMEM199-CDG:** Altered levels of liver-made enzymes (a type of proteins that help chemical reactions happen), altered coagulation parameters, altered copper metabolism (processing, transport) and levels
CCDC115-CDG: Enlarged liver, enlarged liver and spleen (hepatosplenomegaly), impaired bile flow (cholestasis), elevated transaminases, altered copper metabolism (processing, transport) and levels, liver fibrosis, cirrhosis and fatty liver.

ATP6AP1-CDG: Enlarged liver, enlarged liver and spleen (hepatosplenomegaly), jaundice (yellowing of the skin and the whites of the eyes), elevated transaminases, liver fibrosis, fatty liver and cirrhosis.

CDG with minor liver affectation

PMM2-CDG: Enlarged liver, coagulopathy (defects in the blood coagulation mechanism), elevated transaminases, liver fibrosis and fatty liver.

ALG1-CDG: Enlarged liver, altered coagulation parameters, elevated transaminases.

ALG3-CDG: Enlarged liver, elevated transaminases, liver fibrosis, fatty liver and cirrhosis.

ALG6-CDG: Enlarged liver, enlarged liver and spleen (hepatosplenomegaly) and jaundice (yellowing of the skin and the whites of the eyes).

ALG8-CDG: Enlarged liver, enlarged liver and spleen (hepatosplenomegaly), impaired bile flow (cholestasis), coagulopathy (defects in the blood coagulation mechanism), elevated transaminases, liver fibrosis and fatty liver.

ALG9-CDG: Enlarged liver, enlarged liver and spleen (hepatosplenomegaly), altered coagulation parameters.

PGM1-CDG: Enlarged liver and elevated transaminases.

COG1-CDG: Mildly enlarged liver.

COG2-CDG: Altered copper metabolism (processing, transport) and levels

COG4-CDG: Elevated transaminases and cirrhosis.

COG5-CDG: Enlarged liver, jaundice (yellowing of the skin and the whites of the eyes), elevated transaminases.

COG6-CDG: Enlarged liver, enlarged liver and spleen (hepatosplenomegaly), impaired bile flow (cholestasis), elevated transaminases, liver fibrosis and cirrhosis.

COG7-CDG: Enlarged liver, enlarged liver and spleen (hepatosplenomegaly), impaired bile flow (cholestasis), altered coagulation parameters, elevated transaminases and liver cirrhosis.

Taking into account our findings, we recommend that a liver check-up should be performed in all CDG patients with and without known liver problems, so that a greater understanding of the frequency, onset and evolution of liver disease in CDG patients can be achieved.