# Study of N-glycosylation and coagulation during pregnancy in a patient with MPI-CDG treated with mannose supplementation

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## Introduction

### 1) MPI-CDG

Congenital Disorders of Glycosylation (CDG) are a rapidly expanding group of rare inherited metabolic disorders, with over 160 distinct subtypes characterized to date. Among these, MPI-CDG (CDG-Ib) is caused by a deficiency in mannose phosphate isomerase (MPI) due to mutations in the *MPI* gene. This enzymatic defect disrupts the biosynthesis of GDP-mannose and lipid-linked oligosaccharide precursors—essential intermediates in the synthesis of N-glycans—thereby impairing the N-glycosylation process. Oral D-mannose supplementation has been widely implemented for MPI-CDG patients and is known to greatly improve clinical manifestations. Historically, mannose supplementation was discontinued during pregnancy in MPI-CDG patients. However, recent evidence suggests that treatment interruption can have detrimental effects on hemostasis. For the first time, this study reports the biological follow-up of an MPI-CDG patient who continued oral D-mannose supplementation throughout her pregnancy [1].

### 2) Clinical presentation

- ♀
- Diagnosis made at the age of 4 months
- Hypoglycemia, Hyperinsulinism
- Diarrhea → dehydration
- Undernutrition

### 3) Glycosylation study

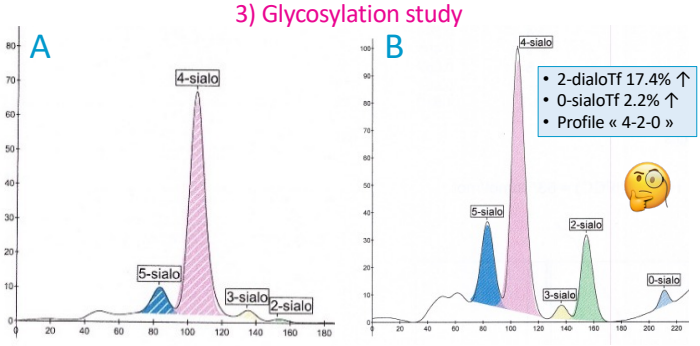
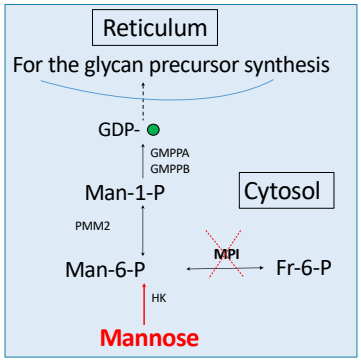



**Figure 1: Transferrin glycosylation profiles of control serum (A) and patient (B)**
**A**. A majority of 4-sialotransferrin. **B**. Compared to control serum, the patient profile presents an elevation of 2-sialotransferrin and 0-sialotransferrin fractions.

→ Evocative profil of a CDG type 1

### 4) Existent treatment

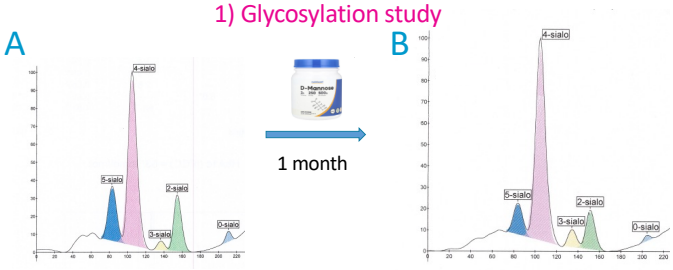
- Treatment: D-mannose oral bypass this enzymatic pathway
- 15 patients followed in 2025 in France [2]
- 0.17-0.2g/kg/day, 3 to 6 times a day, well absorbed, half-life: 4 hours, efficiency +++
- BUT : digestive disorder AND 6-12 g/j for 10 kg or 42 to 84 g/j for70 kg is equivalent to 15.3 to 60.6 kg a year, so compliance is the main issue +++




- The patient reached 28 years old
- Expressed a wish of pregnancy
- Compliance problem with mannose (stopped it)
- Recent history of another pregnant MPI-CDG patient without mannose => veinous thrombosis, cerebral ischemia [3]
- Pluridisciplinary decision for a resumption of low dose of mannose along the pregnancy
- Mannose 4g/day then 8g/day + Enoxaparin sodium 0.6/12h => normal hemostasis

## Results

### 1) Glycosylation study




### 2) Tf glycoforms ratio along the treatment during the pregnancy

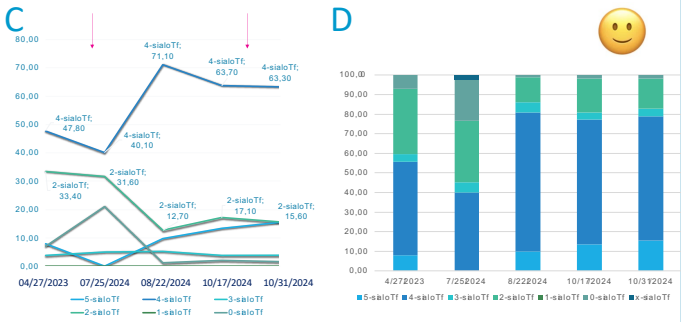
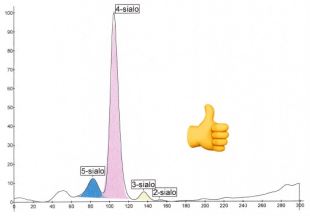



**Figure 2: Transferrin glycosylation profiles of the patient serum before treatment (A), after a month of treatment (B), evolution of the Tf fractions along the pregnancy (C-D)**
**A.** CDT : 19.6 % (2-sialo = 17.4)+(0-sialo= 2.2) **B**. CDT : 9.4% (2-sialo =8.9)+(0-sialo = 0.5).
**C-D.** Resumption of mannose 4g/day on 10/25/2023 (pink arrows). Dose increased to 8g/day on 10/11/2024. Elevation of 4-sialo while 2- and 0-sialotransferrin decrease at the end of the pregnancy.

→ Improvement of glycosylation

## Child profile

- Successful delivery (labor was induced due to IUGR)
- A baby girl weighing 2.390 kg, Apgar scores were 2-2-2-4, requiring neonatal monitoring for a few days
- Both mother and baby are now doing well
- Continuation of curative anticoagulation for 3 months + Mannose at 12 g/day for the mother




| Nom | % |
|---|---|
| 5-sialo | 11,4 |
| 4-sialo | 85,1 |
| 3-sialo | 3,3 |
| CDT (2-sialo = 0,2) | 0,2 |

→ The child present a normal glycosylation profile (as expected in a autosomal recessive disease)

## Conclusion

This case illustrates that the treatment of MPI-CDG patient during the pregnancy by low doses of mannose is safe for the child, improves the compliance of the mother, prevent post-partum thrombosis (as seen in previous case of a MPI-CDG patient's pregnancy without mannose).

## References

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