PMM2-CDG guidelines and standards of care

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What are clinical guidelines?

- Recommendations for clinicians about the care of patients with specific conditions.

- Based upon the best available research evidence and practice experience.

Why are they important and to which ends can they be used?

- To standardize the patients' care among health care providers.
- Accessible tool to general practitioners and families who deal with those patients.

PMM2-CDG guidelines

Introduction

- The initiative to establish guidelines for PMM2-CDG was taken at the International Scientific CDG Symposium, July 2017.

J Inherit Metab Dis. 2019 Jan;42(1):5-28. doi: 10.1002/jimd.12024.

International clinical guidelines for the management of phosphomannomutase 2-congenital disorders of glycosylation: Diagnosis, treatment and follow up.

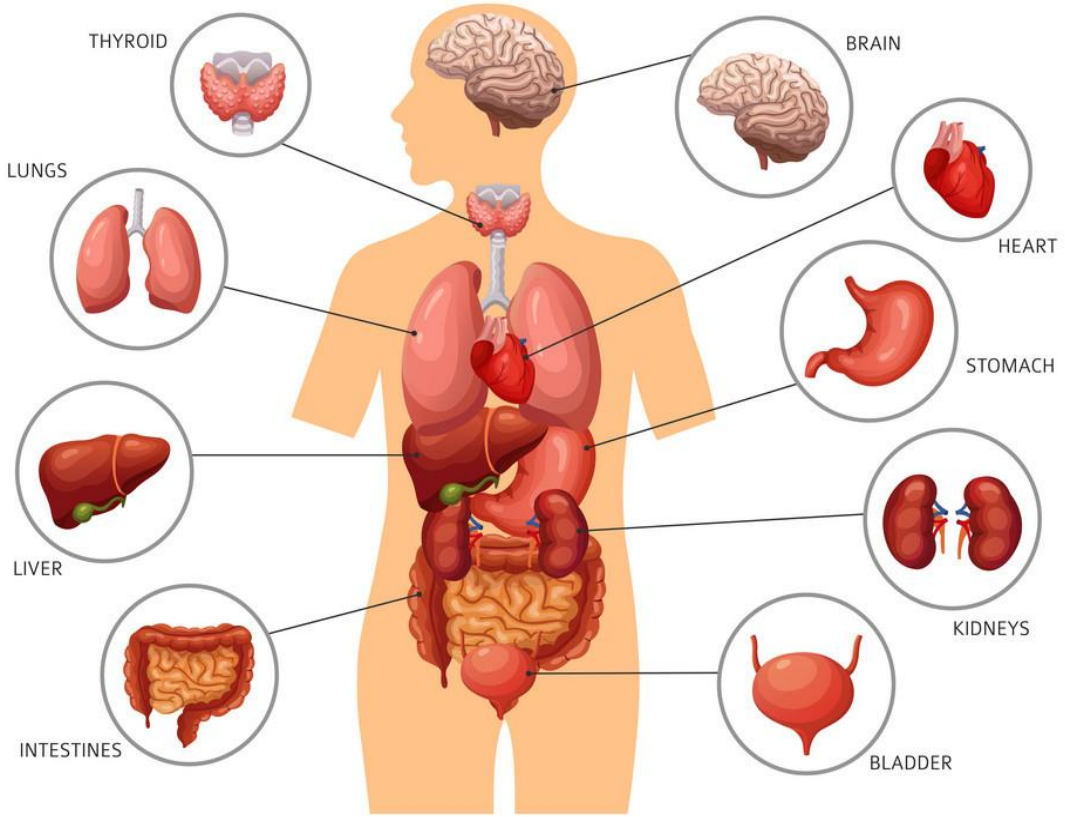
Altassan R[1,2], Péanne R[3,4], Jaeken J[3], Barone R[5], Bidet M[6], Borgel D[7], Brasil S[8,9], Cassiman D[10], Cechova A[11], Coman D[12,13], Corral J[14], Correia J[15], de la Morena-Barrio ME[16], de Lonlay P[17], Dos Reis V[8], Ferreira CR[18,19], Fiumara A[5], Francisco R[8,9,20], Freeze H[21], Funke S[22], Gardeitchik T[23], Gert M[4,24], Girad M[25,26], Giros M[27], Grünewald S[28], Hernández-Caselles T[29], Honzik T[11], Hutter M[30], Krasnewich D[18], Lam C[31,32], Lee J[33], Lefeber D[23], Marques-de-Silva D[9,20], Martinez AF[34], Moravej H[35], Õunap K[36,37], Pascoal C[8,9], Pascreau T[38], Patterson M[39,40,41], Quelhas D[14,42], Raymond K[43], Sarkhail P[44], Schiff M[45], Seroczyńska M[29], Serrano M[46], Seta N[47], Sykut-Cegielska J[48], Thiel C[30], Tort F[27], Vals MA[49], Videira P[20], Witters P[50,51], Zeevaert R[52], Morava E[53,54].

Author information

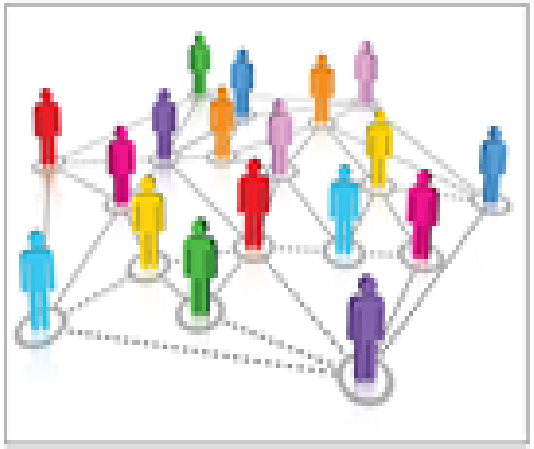
Why PMM2-CDG ?

- PMM2-CDG is the most common congenital disorder of N glycosylation.
- Panethnic disorder.
- More than 900 patients reported worldwide.
- Multisystemic disorder.

Organs involved in PMM2-CDG

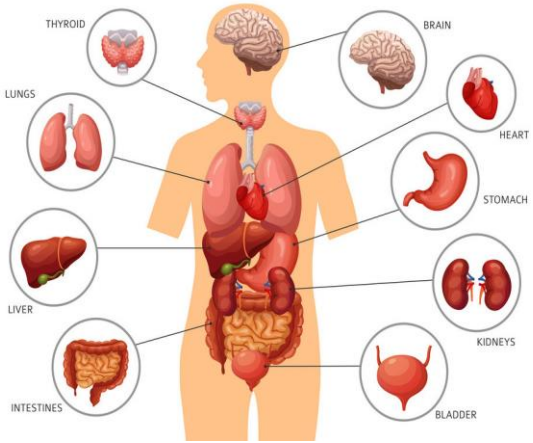


Method



International experts (54 members) divided into clinical and diagnostic groups

>150 peer-reviewed paper



Statements written based on major organs involvement

Results

- Summaries of the phenotypes and proposed recommendations ordered by systems involvement
- Recommendation include the presentation, diagnosis, follow up and treatment
- Suggested surveillance for PMM2-CDG patients (refer to the guideline)

Selected recommendation

Gastroentology

- Presentation: failure to thrive secondary to feeding difficulties, i.e., vomiting, diarrhea secondary to malabsorption, or protein losing enteropathy.

Recommendation:

1. Maximal caloric intake (no special food required for PMM2-CDG
2. Feeding assistance by nasogastric tube or gastrostomy tube
3. Antigastroesophageal reflux measures:
4. Evaluation by a gastroenterologist and nutritionist, esp. in the first year of life
5. Speech therapy and oral motor therapy in the patients with feeding difficulties

Selected recommendation

- Hematology:
- Presentation: coagulation abnormalities and thrombosis risk

- Recommendation

1. For thrombotic events follow the guidelines of the American College of Chest Physicians for curative and prophylactic use of antithrombotic therapy.

2. LMWH should be used by individualized dose.

3. Rivaroxaban can be used as an alternative prophylaxis in LMWH nonresponsive patients.

Selected recommendation

Endocrine:

Presentation: abnormal Thyroid function and hypoglycemia.

Recommendation

1. L thyroxine supplementation should be reserved for patients with concomitant elevated TSH and low free thyroxine (clinical hypothyroidism).

2. The management of hypoglycemia should include continuous tube feeding, i.v. glucose infusion, and complex carbohydrates.

3. Oral diazoxide is recommended in case of hyperinsulinemic hypoglycemia.

Selected recommendation

Immunological system:

- Presentation: infections, immunodeficiency, lack of response to vaccination, and hypogammaglobulinemia

Recommendation

1. For Infections, patients must be managed according to good standards of care, with appropriate antibiotic administration, and patients should be followed closely until infection remission.

2. Intravenous administration of immunoglobulins may be considered if infection is not responsive to antibiotic therapy.

Main challenges of implementing clinical guidelines for PMM2-CDG

- Most of the existing studies and reports were nonsystematic with low quality of evidence.
- Lake of detailed information about the patients' presentation, follow up and treatment.
- Combining the available evidence with the experts' opinions helped in establishing these guidelines.

Advantages of the clinical guidelines for PMM2-CDG

- The guideline intended to optimize and standardize the patients care among health care providers.

- Initiative for the clinicians and researchers to work more to discover this disorder and find the best practice to manage it.

Conclusions and future perspectives

Clinical guidelines for other CDG?

- MPI-CDG
- PGM1-CDG

Thank you

Questions!