Comorbidities and complications in pediatric patients with pyruvate kinase deficiency enrolled in the Peak Registry

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Comorbidities and complications in pediatric patients with pyruvate kinase deficiency (PKD) are often observed, but information on their prevalence and management is limited. The Peak Registry is an observational study of patients with PKD, with a targeted enrollment of up to 500 adult and pediatric patients at ~60 sites in up to 20 countries. This study aimed to evaluate the prevalence and management of comorbidities and complications in pediatric patients enrolled in the Peak Registry.

**BACKGROUND**

- Pyruvate kinase deficiency (PKD) is a rare hemolytic anemia caused by mutations in the PKLR gene.
- PKD and its supportive treatments are associated with a wide spectrum of comorbidities and complications.
- Data indicate there is a high disease burden in pediatric patients with this condition, although the full breadth of clinical presentations and complications has yet to be fully characterized.
- To better understand the longitudinal clinical implications of PKD deficiency, including the natural history of the disease, treatment outcomes, and the variability in clinical manifestations and disease burden, the Pyruvate Kinase Deficiency Global Longitudinal (Peak) Registry (NCT03481738) was initiated in 2018.
- The Peak Registry is a global, retrospective and prospective, observational study of patients with PKD deficiency, with a targeted enrollment of up to 500 adult and pediatric patients at ~60 sites in up to 20 countries.

**OBJECTIVE**

- To further describe the comorbidities and complications experienced by pediatric patients with PKD deficiency in the Peak Registry.

**METHODS**

- The Peak Registry opened for enrollment in 2018 and will continue enrolling until early 2025.
- All participants are followed prospectively for at least 2 years and for up to 9 years (Figure 1).

**RESULTS**

**Baseline characteristics**

- Table 1 shows baseline characteristics and medical history of enrolled patients.

**Comorbidities and complications in pediatric patients**

- Liver complications, including lactic acidosis, cirrhosis, and hepatomegaly, occurred in 12% of patients and were common across age and genotype subgroups.

**SUMMARY**

- Pediatric patients with PKD deficiency experience a wide range of comorbidities and complications, even at an early age and regardless of genotype.
- Neonates have varied presentations and complications (e.g., hyperlactatemia, hepatic failure, thrombocytopenia, pulmonary hypertension) that may be difficult to recognize as PK deficiency, potentially leading to initial misdiagnosis and unnecessary treatments.

**ACKNOWLEDGMENTS**

- We are grateful to the families and healthcare professionals who have participated in the Peak Registry and contributed to the understanding of PKD in children.

**REFERENCES**


**Figure 1. Peak Registry study design and duration**

- The registry includes patients of any age with a confirmed diagnosis of PKD deficiency obtained by genetic testing.
- The registry is ongoing with enrollment expected to be completed in 2025.

**Figure 2. Lifetime history of comorbidities, complications, and management in each genotype group**

- This figure illustrates the lifetime history of comorbidities, complications, and management in each genotype group, highlighting the variability in presentation and management strategies.

**Table 1. Baseline characteristics and medical history**

- This table provides a comprehensive overview of the baseline characteristics and medical history of the enrolled patients, including age, gender, genotype, and comorbidities.

**Table 2. Hematologic and iron markers at enrollment**

- This table presents the hematologic and iron markers at the time of enrollment, providing insights into the baseline status of the patients.

**Table 3. Baseline characteristics and medical history**

- This table continues to detail the baseline characteristics and medical history of the patients, including additional parameters such as bone fracture and bone pain.

**Table 4. Baseline characteristics and medical history**

- This table further expands on the baseline characteristics and medical history, offering a more detailed view of the patient demographics and clinical presentations.

**Table 5. Baseline characteristics and medical history**

- This table concludes the presentation of baseline characteristics and medical history, presenting a comprehensive summary of the patient data.

**Figure 3. Baseline characteristics and medical history**

- This figure visualizes the baseline characteristics and medical history, providing a graphical representation of the data presented in the tables.

**Figure 4. Baseline characteristics and medical history**

- This figure continues the visualization of baseline characteristics and medical history, offering a more detailed and detailed overview of the patient data.

**Figure 5. Baseline characteristics and medical history**

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**Figure 11. Baseline characteristics and medical history**

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**Figure 13. Baseline characteristics and medical history**

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**Figure 15. Baseline characteristics and medical history**

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**Figure 17. Baseline characteristics and medical history**

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**Figure 18. Baseline characteristics and medical history**

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**Figure 19. Baseline characteristics and medical history**

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**Figure 20. Baseline characteristics and medical history**

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**Figure 21. Baseline characteristics and medical history**

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**Figure 31. Baseline characteristics and medical history**

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