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Identifying early indicators of mucopolysaccharidosis disorders using UK parent-held child health records

Eva M. Raebel[1], Thomas Kenny[1], Sophie Thomas[2], Alex Morrison[1]

1. Rare Disease Research Partners*, Amersham, UK; 2. The Society for Mucopolysaccharide and Related Diseases, Amersham, UK

Background

Delays between symptom onset and diagnosis have been reported for all types of mucopolysaccharidosis (MPS) disorders.[1] Preliminary research undertaken by the MPS Society suggested individuals with MPS disorder had a high birth weight.

There is a need for all clinicians who see children to be alert to signs of MPS disorders, so that patients can benefit from an early diagnosis, improve their long-term prognosis and benefit from early treatments, where available.

The Personal Child Health Record (Red Book)

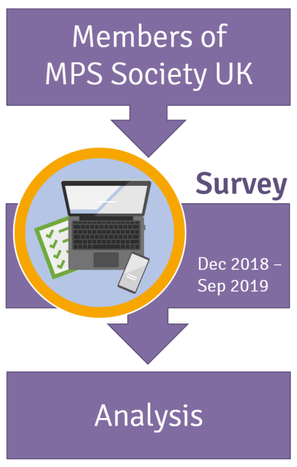
The Personal Child Health Record (PCHR; Red Book) is a UK national standard personal record of a child's health and development. Parents and health professionals can record, for the first years of the child's life, their weight, height, head circumference, milestones and vaccinations.

The Red Book, introduced in the early 1990s, is regularly updated and has been recently launched online.[2]

Objectives

- To examine the early signs or symptoms noted in children subsequently diagnosed with MPS disorders to investigate birth and growth patterns.

Methods



Parents/caregivers of members with MPS were invited to take part in the study by clicking on a link to consent and to undertake the online survey.

The survey was accessed via a hyperlink and completed online through Qualtrics[XM]. It included 34 questions based on self-reported and validated data recorded in their child's Red Book, including photographs of specific sections. This analysis comprises a subset of responses.

The number of received responses varied for each question hence analysis was undertaken individually for each of the questions (e.g. n=47). Female data was scarce hence only male growth charts are reported in this study.

Results

Patient demographics

48 Respondents

48 patients; 25% female

Mean age (±SD): 11.7 (±6.9) years (range 3.6–33.0)

9 MPS disorders/ subtypes (Table 1)

Table 1. MPS disorders/subtypes and age at diagnosis (n=47).

MPS disorder	N	Mean age at diagnosis (yrs)	
MPS I Hurler	8	0.8	±0.5
MPS I Hurler Scheie	1	3.8	–
MPS II Hunter	6	4.5	±2.1
MPS IIIA Sanfilippo	10	3.8	±1.9
MPS IIIB Sanfilippo	3	2.6	±1.2
MPS IIIC Sanfilippo	1	3.0	–
MPS IVA Morquio	13	2.8	±1.8
MPS IVB Morquio	1	9.0	–
MPS VI Maroteaux Lamy	4	3.5	±3.8
Total population	**47**	**3.1**	**±2.3**

Growth patterns

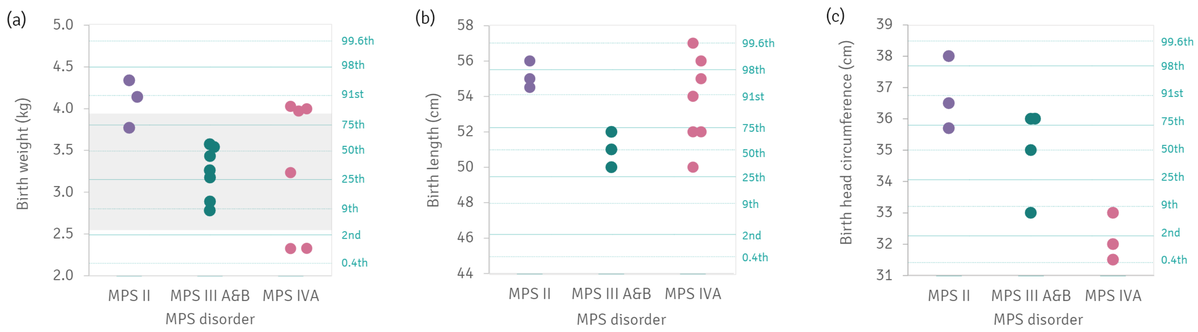


Figure 1. (a) Birth weight (kg) of males (n=17) born at full-term. Shaded area shows normal birthweight range (≥2.5–≤4.0kg). (b) Birth length (cm) of males (n=13) born at full-term. (c) Birth head circumference (cm) of males (n=10) born at full term. Centiles based on UK-WHO Child Growth Standards.[2]

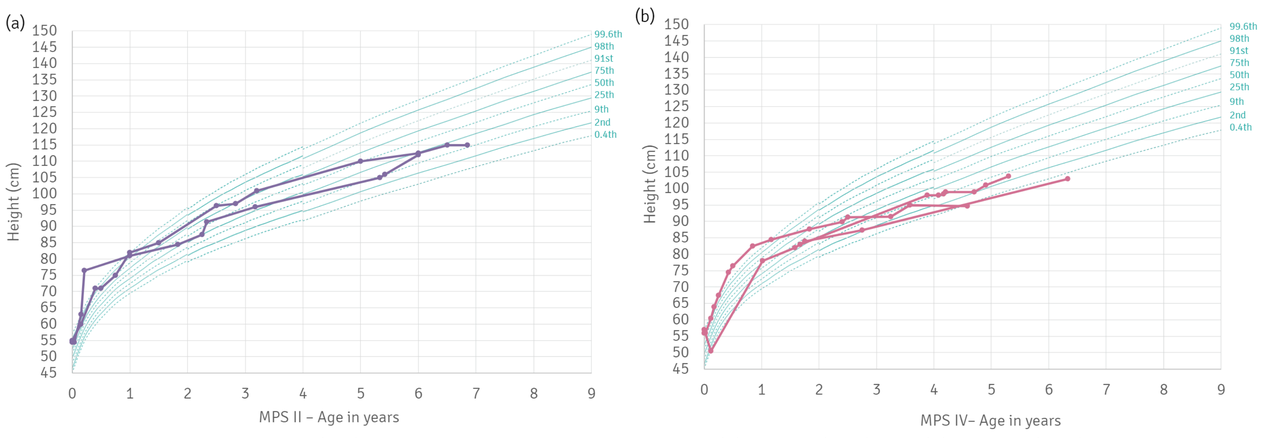


Figure 2. Height (cm) of males from 0–9 years of age for (a) MPS II (n=2) and (b) MPS IV (n=3). Centiles based on UK-WHO Child Growth Standards.[2]

Diagnosis

Mean age at diagnosis (Table 1)

3.1 years

(n=47)

Diagnosed ≤1 year of age

23.4%

(n=47)

Diagnosed after 2 years of age

57.5%

(n=47)

No diagnosis by 5 years of age

17.0%

(n=47)

85.7% of 28 mothers (n=24) noticed something unusual about their child within the first year of life

Key findings

- From 47 children, 58% were diagnosed after the age of 2 years and 17% after 5 years, which has implications for the benefits of early treatment or for eligibility for gene therapy trials.
- Most MPS disorders showed MPS signs and symptoms within the first year, e.g. MPS III and MPS IV, but mean age at diagnosis was 3.1±2.3 years.
- Growth patterns suggested that male MPS II newborns (n=3) were heavy (>75th centile), large (>91st centile) and had a birth head circumference in the upper quartile (>75th centile) (Figure 1). Growth rate started to decrease by the end of their first year (Figure 2a).
- MPS III Sanfilippo male children showed average birth weights (n=7) and lengths (n=3) (25th–75th centiles) (Figure 1) but some children had reached the top centiles in all three variables by 3 years of age.
- Male newborns with MPS IVA (n=6) showed greater variation in birth weights and a small head circumference (Figure 1a&c) however, all fell rapidly off the normal growth charts by the second year of life (Figure 2b).

Conclusions

Birth and growth patterns may aid clinicians who do not often encounter a child with one of these rare disorders to recognise early signs of MPS and to decrease the diagnostic odyssey.

Author's e-mail: e.raebel@rd-rp.com

References: 1. Kuiper G-A, et al. *Orphanet J Rare Dis.* 2018;13(1):2. 2. Personal Child Health record (PCRH). Available from: https://www.who.int/tools/child-growth-standards/standards. Accessed June 2020. **Acknowledgements:** This study was funded by Sanofi Genzyme through a Patient Advocacy Leadership Award. This study was made possible by the participation of the membership of The Society for Mucopolysaccharide Diseases (MPS Society UK) Registered Charity No. 1143472.* MPS Commercial is a Private Limited Company Registered No 08621283. MPS Commercial trades as Rare Disease Research Partners and is a wholly owned, not for profit subsidiary of the Society for Mucopolysaccharide Diseases (the MPS Society), Registered Charity in England and Wales No. 1143472. Rare Disease Research Partners social objectives are to reinvest any surplus to support the mission of the MPS Society to transform the lives of patients through specialist knowledge, support, advocacy and research.