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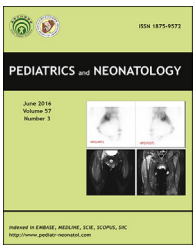

ORIGINAL ARTICLE

Can Macrosomia or Large for Gestational Age Be Predictive of Mucopolysaccharidosis Type I, II and VI?

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Key Words
anthropometric features;
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macrosomia;
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overgrowth

Background: The objective of the study was to compare mean values for birth body length and weight between patients with mucopolysaccharidosis (MPS) and the general population.
Methods: A retrospective analysis of birth anthropometric data was performed for patients ($n = 103$) with MPS I, II, and VI. Two-tailed t tests were used to compare mean values for body length and weight at birth between patients with MPS and the general population.
Results: Mean values for birth body length and weight for all studied groups were greater than in the general population. For body length the differences were statistically significant. When considered individually, 53% of patients were large for gestational age (LGA) and 30% were macrosomic. The highest percentage of LGA was observed in MPS II males and MPS VI females (55% and 56%, respectively), while the highest percentage of macrosomia was observed in MPS VI males (36%).
Conclusion: At the time of birth, MPS patients were larger than those in the general population. High birth weight and/or LGA can be suggestive of MPS disease and should raise suspicion aiding early disease recognition.

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1. Introduction

Mucopolysaccharidoses (MPSs) are a group of lysosomal storage disorders caused by a deficient activity of enzymes responsible for the catabolism of glycosaminoglycans (GAGs) leading to a short stature and severe joint and bone disease.[1] Mucopolysaccharidosis type I (MPS I) is caused by a deficient activity of alpha-L-iduronidase (IDUA; EC 3.2.1.76) and is divided into three subtypes based on the severity of symptoms: Hurler syndrome (severe, OMIM 607016), Hurler—Scheie syndrome (intermediate, OMIM 607015), and Scheie syndrome (attenuated, OMIM 607016).[1—3] Mucopolysaccharidosis type II (MPS II, Hunter disease, OMIM 309900) is an X-linked recessive disorder caused by a deficient activity of iduronate-2-sulfatase (IDS, EC 3.1.6.13). Hunter syndrome affects primarily males while females are nonmanifesting carriers of Condition 1. Mucopolysaccharidosis type VI (MPS VI, Maroteaux-Lamy syndrome, MPS VI, OMIM 253200) is caused by a deficient activity of N-acetylgalactosamine-4-sulfatase (4-sulfatase, arylsulfatase B, ARSB, EC 3.1.6.12).[1,4]

Human growth is a multi-factorial and complex process, involving physiological interplay between nutritional, endocrine, and metabolic factors, on a wider background of variation in genetic traits and environmental exposure.[5] MPS diseases lead to a profound disruption in normal mechanisms of growth and development.[6] The underlying cause of degenerative bone and joint disease is a lack of skeletal remodeling, disordered endochondral and intramembranous ossification, disruption of normal elastogenesis, and the infiltration by GAGs of the ligaments, tendons, joint capsules, and other tissue structures.[7—9] GAG storage in MPS induces a complex sequence of molecular abnormalities leading to inflammation, apoptosis (cartilage), and hyperplasia (synovial membranes), resulting in poorly organized and metabolically abnormal connective tissue matrices.[7,9—11]

In our previous studies, we evaluated and compared growth patterns in patients with MPS I ($n = 14$) and MPS II ($n = 28$).[12—14] In this study, which deals exclusively with birth parameters, additional data as well as MPS VI patients were added to compare birth body length and weight between MPS I, II, VI, and the general population.

2. Methods

2.1. Study participants

A retrospective analysis (years 1989—2012) of birth anthropometric data ($n = 103$) was performed for patients with MPS I (18 boys), MPS II (56 boys), and MPS VI (11 boys and 18 girls). All patients with MPS I and II were of Polish origin, while patients with MPS VI were of Polish ($n = 11$), Russian ($n = 8$), Lithuanian ($n = 6$), Belarusian ($n = 2$), and Estonian ($n = 2$) origin. Birth data were collected from health books of each patient. All measurements were performed at the time of birth, in hospitals where the children were born.

All patients were born at term (prematurely born patients were excluded from the study), and presented typical clinical features of MPS and had a diagnosis of MPS type I, II, or VI confirmed by biochemical and molecular analyses.

All patients were naïve to enzyme replacement therapy (ERT) during the time of the study.

2.2. Study design

The study objectives were to compare mean values for birth body length and weight between patients with MPS I, II, VI, and the general population.[15]

2.3. Anthropometric measurements

Anthropometric measurements were taken according to a standard technique and included body length/height. Length was measured in the supine position using a tape measure. The body weight was measured using an electronic scale accurate to within 0.05 kg.

2.4. Data analysis

Two-tailed *t* tests were used to compare mean values for body length and weight at birth between patients with MPS I, II, VI, and the general population.

2.5. Ethical consideration

The protocol was approved by the Human-subjects Institutional Review Board at the Children's Memorial Health Institute, Warsaw, Poland. A written informed consent had to be provided by parents or legal guardians.

3. Results

Mean values for birth body length and weight for all studied groups were greater than in the general population (Table 1). For body length the differences were statistically significant (Figure 1). LGA was defined as a weight, length, or head circumference that lies above the 90th percentile for gestational age. Macrosomia, which literally means "big body," is defined by the American College of Obstetricians and Gynecologists, as birth-weight $>$ 4000 g or $>$ 4500 g irrespective of gestational age. When considered individually, 53% of patients were large for gestational age (LGA) and 30% were macrosomic. The highest percentage of LGA was observed in MPS II males and MPS VI females (55% and

Table 1 Mean value of body weight and length in the studied population.

No.	Group (*n*)	Body length (cm)	Body weight (kg)
1	MPS I (18)	55.6 ± 3.45	3.47 ± 0.61
2	MPS II (56)	55.4 ± 2.68	3.63 ± 0.56
3	MPS VI		
	Boys (11)	55 ± 3.59	3.82 ± 0.61
	Girls (18)	53.8 ± 2.89	3.62 ± 0.56
4	Healthy population		
	Boys	52.2 ± 2.8	3.50 ± 0.6
	Girls	51.3 ± 2.5	3.4 ± 0.5

Data are presented as mean ± standard deviation.
MPS = mucopolysaccharidosis.