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Assessment of risk factors for osteoporosis and fractures in children with meningomyelocele

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ABSTRACT

Purpose: Our objective was to assess bone and muscular mass in children with meningomyelocele (MMC), and to analyze risk factors for osteoporosis and fractures based on densitometric examination.

Material and Methods: The study group included 30 patients (15 girls and 15 boys) with MMC, aged 6–17 years, treated in the Department of Pediatric Rehabilitation, University Hospital. Physiotherapeutic assessment and laboratory tests (serum parathormone, alkaline phosphatase levels, calcium, and phosphate levels, and urine calcium levels) were performed. Densitometry was measured by dual energy X-ray absorptiometry using a Lunar DPX-L apparatus. Lean mass (fat-free tissue content) and fat mass (% fat content) was evaluated.

Results: Femur fractures were the most common 12/30 (40%); 5/30 (17%) of the children with MMC had multiple fractures. The incidence of fractures correlated significantly with BMI and body fat content ($p = 0.03$) Children with MMC and fractures had a tendency toward higher BMI, despite the same absolute value of body mass, compared to those without fractures. Body fat levels were higher in MMC patients with fractures than in those without fractures (BMI $R = 0.393$, $p = 0.03$). Children with MMC and fractures had significantly higher 24 h calcuria values, despite normal renal function indices ($p = 0.03$).

Conclusions: Low-energetic fractures in MMC children may result from metabolic disturbances that are a consequence of excessive renal calcium loss or excessive fatty tissue content.

Key words: meningomyelocele, children, osteopenia, osteoporosis, densitometric examination, fractures

INTRODUCTION

Meningomyelocele (MMC) is congenital malformation of the neural tube in which the spinal cord and nerve roots herniate through a defect in the vertebral arches. The condition results in varying sensory and motor deficits [1]. In addition to muscle weakness and sensory loss, associated problems include impaired bladder and bowel control, hydrocephalus, and impaired mental development in most of MMC cases. Kinsman *et al.* [2] emphasize that medical care of patients with MMC should have an interdisciplinary nature, with the ultimate aim of achieving maximum functional independence.

MMC is the second most common (after Down syndrome) congenital defect, with an incidence of one in 1,000 live newborns [3,4]. Its incidence in Poland ranges between 2.05 and 2.68 per 1,000 births. It is a nonstabilized defect; enhancement of locomotor disorders is due to asymmetry of pairs of muscles.

New pareses or palsies, as well as loss of sensation, are caused by stretching of the spine and nerve roots due to fusion of nerve elements with the surroundings. The clinical picture of locomotor disorders and originating deformities of the lower limbs depends upon the level of neurosegment injury and upon palsy type [5-7]. The occurrence of complications such as fractures of the extremities below the site of spine damage is related to bone structure disorders. Because the clinical picture of fractures in patients with MMC do not display the classical symptoms, it is often very difficult to establish a definitive

Table 1. **Somatic features of study patients with meningomyelocele (MMC), (n=30).**

Mean body mass of patients without fractures	30.72 ± 15.20 kg
Mean body mass of patients with fractures	38.16 ± 15.77 kg
Mean body height of the patients without fractures	1.29 ± 0.20 m
Mean body height of the patients with fractures	1.33 ± 0.19 m
BMI in the study group of patients without fractures	17.11 ± 3.80
BMI in the study group of patients with fractures	20.64 ± 4.64

BMI- body mass index

diagnosis [7,8]. A negative history of trauma, painless course, local hard edema with skin reddening, and elevated body temperature may lead to an incorrect diagnosis. Fractures cause abnormal movement and deformities. Furthermore, immobilization in plaster (>6 weeks) can exacerbate bone atrophy. Because we consider fractures and osteoporosis to be substantial medical and social problems confronting patients with MMC who are undergoing rehabilitation, we attempted to assess bone mass and muscular mass, and to analyze prognostic factors for fractures based on densitometric examinations.

MATERIAL AND METHODS

The study included 30 patients (15 girls and 15 boys) with MMC aged 6–17 years (mean ± SD 10.56 ± 3.49 years) treated in the Department of Pediatric Rehabilitation and in the Outpatient Department of Rehabilitation and Neurology of the Medical University of Bialystok, Poland, from 1990 to 2005.

Patients with fractures of the lower extremities were identified based on medical history. We then performed neuropediatric and physiotherapeutic physical examinations and locomotor assessments for both ambulant and wheelchair-using patients. The following laboratory test results were collected: serum parathormone (PTH), alkaline phosphatase (ALP), calcium, and phosphate levels, and 24 h calcium excretion in urine. Anthropometric parameters were measured (body height ± 0.2 cm using a wall-mounted stadiometer or a centimeter measure in prone patients; body mass ± 0.01 kg by an electronic weighing scale).

Body mass index (BMI) was calculated according to the formula BMI = body mass (kg)/height^2 (m^2). Densitometry was measured by the dual energy X-ray absorptiometry (DXA) method using a Lunar DPX-L apparatus (GE Medical Systems-Lunar Radiation Corporation). DXA measurement of the entire skeleton was carried out to assess total bone mineral density (total BMD) and body components (lean mass, fat-free tissue content; fat mass, % fat content), and at the level of lumbar vertebrae L1–L4 in anteroposterior projection (skeletal area of lumbar spine BMD; expressed in g/cm^2 in percentiles according to age and gender norms). BMD values were calculated from the mineral density expressed in grams within the total measurement area (bone mineral content [BMC]) divided by the surface area, and expressed as Z scores (Z total; the number of standard deviations that the distinguished bone density of the affected patient from that of a statistically healthy subject matched by gender, race, and age). The radiation dose in the study did not exceed 7 μSv, and was safe. The study was approved by the Bioethical Committee of the Medical University of Bialystok.

Statistical analysis was performed using the following tests: Student's *t*-test for independent samples, Spearman's test, Wilcoxon's test, Chi^2 test with Yates' modification, and Fisher's test.

RESULTS

1.Age of study patients with MMC

The mean age of the study patients without fractures was 10.3 ± 3.76 years for those without fractures, and 10.9 ± 2.84 years for those with fractures (*Tab. 1*). The difference was not statistically significant (p = 0.855). On average, the fractures occurred between two and three years of age. No differences were noted in the incidence of fractures between girls and boys: six girls and six boys had bone fractures (p = 0.746), whereas nine girls and nine boys did not (p = 0.746).

2. Somatic features of study patients with MMC

Tab. 1 lists the somatic features of study patients with MMC and a positive or negative history of fractures of the lower extremities. Differences in the mean body mass and height of patients with and without fractures were statistically insignificant (*Tab. 1*). There was no correlation between body mass and fractures of the lower extremities in MMC patients results are shown (*Tab. 2*). The average BMI of the groups without and with fractures was 17.11 ± 3.80 and 20.64 ± 4.64, respectively; the difference was statistically insignificant (p = 0.084) (*Tab. 1*). The correlation between BMI and the incidence of fractures of the lower extremities in MMC patients was statistically significant (R = 0.393, p = 0.03) (*Fig. 1*).

3. Lower extremity fractures in patients with MMC at thoracolumbar or lumbosacral segments

There was no relationship between MMC at the thoracolumbar (Th/L) segment and the incidence of fractures (R = 0.0321; p = 0.865), nor between MMC at the lumbosacral (L/S) segment and fractures of the lower extremities (R = −0.0321, p = 0.865).

Figure 1. **Correlation of fractures of the lower extremities with BMI in meningomyelocele (MMC) (n=30) patients.**

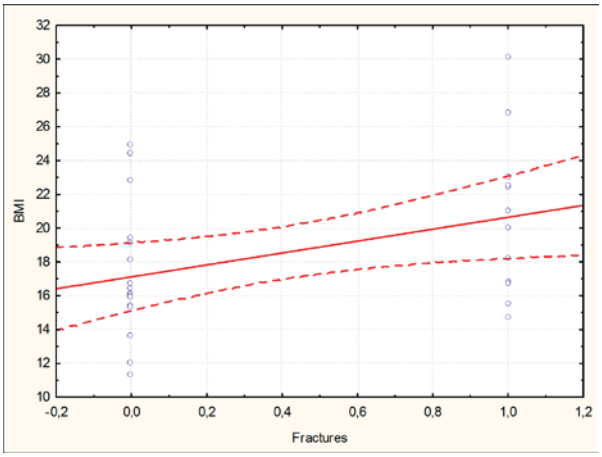
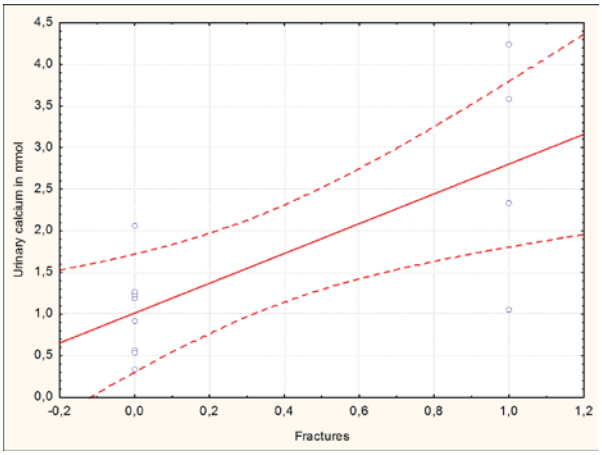


Figure 3. **The correlation between the incidence of fractures in meningomyelocele (MMC) patients (n=30) and the urinary level of calcium in a 24h urine sample.**



4. Laboratory values for PTH, ALP, and calcium excretion

Serum concentrations of PTH (a hormonal regulator of the calcium–phosphate balance) and ALP in MMC patients with and without fractures are presented in *Fig. 2*. The mean PTH level in patients without fractures was 57 ± 35.4 pg/ml, whereas in patients with fractures it was 61 ± 38.1pg/ml (reference values 15–65 pg/ml). The difference between the two groups was not statistically significant (p = 0.7353). No correlation was found between PTH levels and fractures of the lower extremities (R = 0.070, p = 0.760) (*Tab. 2*). The level of serum ALP was 205.14 ± 97.22 U/L (reference values 110–360 U/L) in MMC patients with a negative history of fractures, and 223.66 ± 88.33 U/L in patients with fractures. The difference was not statistically significant (p = 0.116). There was a significant correlation between the incidence of fractures in MMC children and increased levels of calcium in a 24 hour urine sample (Spearman's test R = 0.6145, p = 0.033) (*Fig. 3*).

Figure 2. **Serum levels of parathormone (PTH) and alkaline phosphatase (ALP) in the study patients with meningomyelocele (MMC) (n=30).**

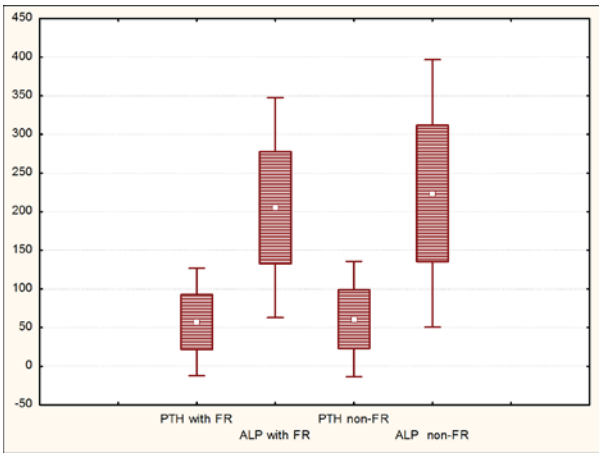


Table 2. **Correlations of fractures in children with risk factors for meningomyelocele (MMC) (n=30) in Spearman's test.**

Fractures and PTH	R=0.070	p=0.760
Fractures and body mass	R=0.279	p=0.134
Fractures and height	R=0.082	p=0.664
Fractures and BMI	R=0.393	p=0.031
Fractures and walking	R=-0.305	p=0.100
Fractures and living in a wheelchair	R=0.305	p=0.100
Fractures and BMD	R=0.068	p=0.732
Fractures and Z- Tot	R=0.206	p=0.300
Fractures and SP BMD	R=-0.157	p=0.432
Fractures and Z- SP	R=-0.137	p=0.492
Fractures and Fat %	R= 0.157	p=0.432
Fractures and Fat g	R=0.157	p=0.432
Fractures and Lean g	R=0.0098	p=0.961
Fractures and Lean Arms	R=0.0098	p=0.961
Fractures and Lean Legs	R=-0.049	p=0.807
Fractures and BMC g total	R=0.000	p=1.00
Fractures and BMC Arms	R=0.068	p=0.732
Fractures and BMC Legs	R=- 0.098	p=0.625
Fractures and BMC Trunk	R=0.049	p=0.807

PTH - parathormone, BMI - body mass index, SP - spine, BMD - bone mineral density, BMC - bone mineral content

5. Locomotor activity and incidence of fractures

No differences were found in the incidence of fractures of the lower extremities among ambulant MMC patients; six of the 12 patients with fractures and 12 of the 18 patients without fractures were ambulant (Fisher's test p = 0.776). Similarly, there were no differences in wheelchair use between the fracture (6/12 patients) and nonfracture (6/18 patients) groups (p = 0.713). No correlation was observed between the level of locomotor activity and the incidence of fractures of the lower extremities (R= −0.305, p = 0.100) (*Tab. 2*).

6. Densitometric examination of patients with MMC

The mean BMD in the nonfracture group was 0.86 ± 0.13 g/cm^2, whereas in the fracture group it was 0.90 ± 0.12 g/cm^2. No differences were noted for BMD between the two groups (Student's *t*-test $p = 0.485$) (*Tab. 2*). In the MMC patients without fractures, the mean Z score for total BMD was −0.59 ± 1.17; in the patients with fractures, it was −0.032 ± 1.26. There were no significant differences in total BMD Z scores between the fracture and nonfracture groups ($p = 0.423$).

In the nonfracture group, the spine BMD was 0.85 ± 0.13 g/cm^2, whereas in the fracture group it was 0.54 ± 0.30 g/cm^2. There were no significant differences in spine BMD scores between MMC patients with fractures and those without fractures ($p = 0.423$). In the nonfracture group, the spine BMD Z score was −2.63 ± 2.84, while in the fracture group it was −2.30 ± 2.00. There were no significant differences between the fracture and nonfracture groups for spine BMD Z scores ($p = 0.21$).

In the nonfracture group, the mean percentage of total fat was 22.35 ± 9.37%, whereas in the fracture group it was 36.21 ± 17.24%. No differences were found. There was no significant difference in percentage of total fat between the groups. In the nonfracture group, the mean total grams of fat was 6,932.00 ± 4,888.99 g, whereas in the fracture group it was 14,859.45 ± 12,468.11 g. There were no significant differences in the total grams of fat between the fracture and nonfracture groups of MMC patients ($p = 0.061$).

The mean total lean tissue content of the nonfracture group was 44,429.13 ± 8,781.60 g, while in the fracture group it was 22,237.91 ± 8,002.99 g. No significant differences were noted in the total lean tissue content between patients with and without fractures ($p = 0.789$). In the nonfracture group, the mean amount of lean leg tissue was 7,046.75 ± 3,980.55 g; in the fracture group it was 6,792.45 ± 3,204.62 g. There was no significant difference in the leg lean tissue content between MMC patients with and without fractures ($p = 0.858$).

In the nonfracture group, the mean total BMC was 1,165.87 ± 688.27 g, whereas in the fracture group it was 1,263.0 ± 577.66 g. No differences were found in the total BMC between MMC patients with and without fractures ($p = 0.593$).

7. BMC of arms, legs, and trunk

The mean BMC of arms in the group of patients without fractures was 162.18 ± 125.68 g; in the fracture group it was 168.27 ± 101.22 g. There was no significant difference in the BMC of arms between the two groups ($p = 0.533$). In the nonfracture group, the mean BMC of legs was 302.37 ± 253.43 g, while in the fracture group it was 297.27 ± 231. 84 g. No significant differences were found in the BMC of legs between the two groups ($p = 0.656$). In the group of MMC patients with no fractures, the mean trunk BMC was 364.75 ± 253.49 g, whereas in the group with fractures it was 430.63 ± 252.55 g. No significant differences were noted in the trunk BMC between the fracture and nonfracture groups ($p = 0.504$).

DISCUSSION

In our study, fractures affected both genders equally. No correlations were noted between bone mass and incidence of fractures in children with MMC. The lean body mass in boys and girls with MMC who had sustained fractures was similar to that in children with MMC who had never had a fracture. However, children with MMC and fractures had a higher BMI and more body fat compared to those with MMC and a negative history of fractures.

Osteoporosis is a systemic disease of the skeleton characterized by low bone mass and impaired microarchitecture of the bone tissue; as a consequence, affected bone is and susceptible to fractures. In growing children, care should be taken to distinguish osteoporosis, as it is commonly defined above, from other forms of abnormal bone mineralization [10]. In 2001, the National Osteoporosis Foundation and the American National Institutes of Health proposed the following new definition for osteoporosis: it is a skeletal disease characterized by impaired bone endurance, which results in increased risk of fracture [11]. Taking into account the fact that densitometric examination is not completely reliable and that bone volume measurement in particular is not completely objective, diagnoses of osteoporosis in growing children should be based on findings revealed by a combination of investigations, including clinical observation, biochemical markers of bone metabolism, X-rays, and densitometry. The accepted criterion for a diagnosis of osteoporosis based on the results of densitometry is a reduction in bone density by more than two standard deviations compared to the mean for age and gender (Z score < −2.0) [12]. Osteopenia is indicated by an arbitrary range of Z scores between −1.0 and −2.0 SD compared to statistical findings for a healthy subject of the same gender, race, and age [13]. Body mass, height, and BMI also seem to affect BMD. Lorenc *et al.* emphasize that not only anthropometric parameters but also lean tissue and muscle mass index should be analyzed to properly interpret densitometric findings [14-16]. In groups of patients with MMC and with or without fractures of the lower extremities, no significant correlations were observed with somatic features, although higher BMI percentile values were noted among children with fractures.

Bone endurance is a measure of bone mineral density and quality. In a normally developing child, learning to walk is critically important to the development of the osteoarticular system. Constant burdens and pressure forces placed on bones are indispensable for the formation of normal osseous tissue, ensuring its durability and endurance. Low physical activity, because of the lack of bone burden, seriously hinders the formation of normal structures, and long-term immobilization contributes greatly to the development of secondary osteoporosis. The osseous system undergoes dynamic transformations, in which resorption and osteogenesis sequentially determine the ultimate bone shape. In childhood

and adolescence, the predominance of osteogenesis over resorption contributes to skeletal growth. Its ultimate structure depends on a number of factors, such as genetic determinants, general health condition, nutrition status, and physical activity [12]. In the analyzed group of patients, the incidence of fractures did not correlate with locomotor activity (ambulant patients versus those using a wheelchair) or with such risk factors as age or female gender, although, as reported by Valtonen *et al.*, the risk of fractures is significant in patients with MMC and low physical activity and neurogenic bladder [17]. In the present study, we found no significant correlation between fracture incidence and MMC location. However, most authors suggest that patients with MMC have a predisposition to fractures of the thoracic and upper lumbar segments due to their neurological deficits [18-20].

Our results support the findings reported by other researchers regarding healthy populations of children and adolescents, in which fractures are significantly more common among those who are overweight [21,22]. However, the mechanism and character of this association is probably different in our study group, most because of their different levels of movement and activity (predominantly sedentary life style, limited movement, and lack of lower limb burdening). Because fractures in our study participants had no association with activity, locomotion, clinical picture, or level/anatomical location of the hernia, increased fat deposition and excessive body mass may contribute to the pathomechanism of bone fragility in MMC children. Gravity loading was not involved in the mechanism of fractures in these children; all of the fractures were due to small traumatic forces. No relationship was found between fractures and basic indices of calcium metabolism. PTH, calcium, Ca^{2+}, phosphates, and ALP in blood serum did not differ between children with and without fractures. However, children with MMC and fractures were found to have significantly higher values of 24 h calcuria, despite normal renal function indices, a lack of features indicating active infection of the urinary system, or treatment that would affect urinary calcium loss. Excessive calcuria suggests that a renal mechanism may be involved in increased bone fragility in children with fractures; however, what this mechanism might be is unknown, necessitating further investigation. Prospective studies are needed to determine whether patients with MMC are at increased risk of osteoporotic fractures in adulthood, which would be a considerable obstacle to rehabilitation.

CONCLUSIONS

Fractures of the lower extremities in children with MMC may be the result of metabolic disturbances, which could be a consequence of calcuria or excessive amounts of fatty tissue.

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