

Assessment of nutritional status of children with portal hypertension

Ocena stanu odżywienia u dzieci z nadciśnieniem wrotnym

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Abstract

Introduction: Assessment of nutritional status of children with portal hypertension is an important prognostic factor which plays a significant role in the efficacy of their treatment.

Aim: To assess the nutritional state of paediatric patients with portal hypertension through various methods of nutritional assessment and to investigate the usefulness of the techniques.

Material and methods: The study group included 31 children with portal hypertension classified into 3 subgroups: patients with portal vein obstruction, biliary cirrhosis and post-hepatic cirrhosis. The following anthropometrics data were measured: weight, body mass index (BMI), Cole's index and body mass rate (BMR). The body fat (BF) and fat-free mass (FFM) were measured by skin fold bioelectrical impedance assessment (BIA) and dual-energy X-ray absorptiometry (DEXA). The total body water percentage (TBW%) and extracellular fluid content were measured by bioelectrical impedance (BIA). Laboratory parameters such as albumins, cholesterol, vitamin levels (A, E and D), and trace elements (Fe, Zn) together with other biochemical markers were also assessed. The control group consisted of healthy children selected according to their age.

Results and conclusions: Malnutrition, based on Cole's index and BMI < 10th percentile, was detected in 60% of children with biliary cirrhosis, 55.5% of those with post-hepatic cirrhosis and 45.5% of those with portal vein obstruction, respectively. Fat-free mass, measured by different methods, remained stable in each group ($r = 0.97$). For BF, the correlation between anthropometry, BIA and DEXA was significantly lower. Total body water percentage was higher in children with biliary cirrhosis than in other groups ($p < 0.05$). Vitamin A concentration was decreased in each

Streszczenie

Wstęp: Stan odżywienia u dzieci z nadciśnieniem wrotnym odgrywa ważną rolę w skuteczności terapii oraz rokowaniu. Bardzo ważne znaczenie ma wczesne wykrycie zaburzeń stanu odżywienia i odpowiednie leczenie żywieniowe w tej grupie pacjentów.

Cel: Ocena stanu odżywienia u dzieci z nadciśnieniem wrotnym z zastosowaniem różnych metod, a także określenie ich przydatności w diagnostyce.

Materiał i metody: Grupę badaną stanowiło 31 dzieci z nadciśnieniem wrotnym, które podzielono na 3 podgrupy, w zależności od etiologii choroby: pacjentów z blokiem przedwątrobowym, marskością żółciową oraz marskością pozapalną. We wszystkich grupach wykonano następujące badania: pomiary antropometryczne (masa ciała i wysokość), wskaźnik masy ciała (BMI), wskaźnik Cole'a i współczynnik masy ciała (WMC). Dodatkowo u wszystkich obliczono beztłuszczową masę ciała (BMC) oraz masę tłuszczową na podstawie pomiaru 4 fałdów skórnych (nad mięśniami: dwugłowym, trójgłowym oraz pod łopatką i nad kolcem biodrowym). Oceny dokonano metodą bioelektrycznej analizy impedancji (BIA) oraz metodą podwójnej absorpcji promieniowania X (DEXA). Zawartość wody całkowitej (CW) i wody zewnątrzkomórkowej (ZW) w organizmie oszacowano metodą bioelektrycznej analizy impedancji (BIA). Wykonano również badania laboratoryjne z krwi: oznaczenie stężenia albumin, cholesterolu, witaminy A i E, 25-hydroksycholekaliferolu oraz pierwiastków śladowych (Fe, Zn). Grupę kontrolną stanowiły zdrowe dzieci w podobnym przedziale wiekowym.

Wyniki i wnioski: Niedożywienie, opierając się na wskaźnikach Cole'a i BMI < 10. percentyla, zidentyfikowano u 60% dzieci z marskością żółciową, 55,5% z marskością pozapalną i 45,5% z blokiem przedwątrobowym. Oceniając BMC różnymi metodami, uzyskano zbliżone wyniki, nieróżniące się staty-

group (the lowest in children with biliary cirrhosis). No correlation between aminotransferase concentration and nutritional state was found.

Introduction

Portal hypertension refers to abnormally high pressure in the hepatic portal vein. It is defined as a portal pressure of 12 mmHg or more (compared with the normal 5-10 mmHg) [1]. A consequence of the obstruction through the portal vein is the development of collateral circulation. Portal hypertension can occur in children with any type of chronic liver disease which causes cirrhosis (intrahepatic blood flow obstruction) or in those with portal vein thrombosis leading to its obstruction (extrahepatic portal hypertension). Portal hypertension may affect intestinal function leading to malnutrition in children with liver disease. Other causes of the pathological state are: increased energy expenditure, decreased food intake and metabolic derangements [2]. It is crucial to maintain proper nutritional status in patients awaiting liver transplantation as it has an influence on their growth before the intervention and determines the prognosis after the operation [3]. However, reliable assessment of nutritional status in patients with portal hypertension is difficult, as basic nutritional measurements, such as body mass and height, are not sufficient parameters because of the water retention and ascites frequently found in those patients. In those cases it is essential to assess the body constitution by body fat (BF), fat-free mass (FFM) and water content measurements. Fat-free mass and BF are measured by anthropometric skin fold measurements and dual-energy X-ray absorptiometry (DEXA), while bioelectric impedance assessment (BIA) also enables water content assessment.

Aim

This study aimed to assess the nutritional state of paediatric patients with portal hypertension using various methods of nutritional assessment and to investigate the usefulness of these diagnostics.

Material and methods

Patients

This study included 31 children with diagnosed portal hypertension, hospitalized in the Department of Gastroenterology, Hepatology and Immunology, Children's

stycznie między poszczególnymi metodami ($r = 0,97$). W przypadku masy tłuszczowej korelacje były znacząco mniejsze. Największą zawartość wody całkowitej stwierdzono u dzieci z marskością żółciową. Stężenie witaminy było mniejsze u wszystkich dzieci z nadciśnieniem wrotnym, zwłaszcza w grupie z marskością żółciową. Nie wykazano zależności wykładników stanu zapalnego od parametrów czynności wątroby u dzieci z nadciśnieniem wrotnym.

Memorial Health Institute, Warsaw, Poland. The study was accepted by the Bioethical Commission. Diagnosis was based on portal hypertension manifested by oesophageal varices and obstruction to the flow of the portal vein detected in ultrasonography. Children with intrahepatic disorders (liver cirrhosis) also had history of liver biopsy taken in order to determine disease aetiology.

Patients were divided into 3 subgroups:

- those with portal vein obstruction (extrahepatic portal hypertension);
- those with obstruction to flow on the basis of a biliary tract disease (biliary cirrhosis);
- those with obstruction to flow on the basis of chronic hepatitis (post-hepatitic cirrhosis).

Laboratory tests were carried out during one of the patient's numerous hospitalizations. Inclusion criteria were: portal hypertension, A or B children's group in patients with liver cirrhosis (those in group C were excluded), age 5-18 years. Written informed consent was obtained from parents or children's legal guardians before the study commencement.

Description of study groups

Group 1 – patients with portal hypertension on the basis of portal vein obstruction

Diagnosis was confirmed by Doppler flow ultrasonography and the presence of oesophageal varices in endoscopy. This group consisted of 11 patients (6 males and 5 females) aged 11.5 ± 4.0 years.

Group 2 – patients with portal hypertension on the basis of a biliary tract disease

Intrahepatic obstruction to flow was confirmed by Doppler flow ultrasonography, liver cirrhosis by histopathological examination (biopsy). Presence of oesophageal varices was supplementary evidence of portal hypertension. This group consisted of 11 patients (6 males and 5 females) aged 11.2 ± 3.5 years.

Group 3 – patients with portal hypertension due to HBV infection

Intrahepatic obstruction to flow was confirmed by Doppler flow ultrasonography, liver cirrhosis by histopathological examination (biopsy). Presence of oeso-

phageal varices was supplementary evidence of portal hypertension. This group consisted of 9 patients (8 males and 1 female) aged 13.4 ± 4.3 years.

Description of control groups

The control group was classified into three subgroups consisting of healthy children selected from Warsaw schools according to their age. Group 1 – 336 healthy children to have FFM and BF measured by DEXA method. The mean value of FFM and BF was estimated for each age group. Group 2 – 9 healthy children aged 9.7 ± 2.7 to have FFM and BF measured by BIA method. Group 3 – 9 healthy children aged 9.7 ± 2.7 to have total body water percentage (TBW%) and amount of extracellular fluid assessed by BIA.

Methods

All participants underwent the following examinations:

Anthropometry

Each individual child had height and weight accurately measured on scales (ZALiMP, Warsaw), in hospital, in the morning in the fasting state. The results were compared to standard charts (height/weight for age) and percentile values were determined. To make the results more objective, the following parameters were assessed additionally:

- body mass index (BMI) based on height and weight: mass (kg)/height² (m²); results were compared to standard charts for the age;
- Cole's index to calculate the sensitivity, specificity and agreement of BMI; patient's BMI/standard BMI (50th percentile for body mass/50th percentile for height concerning age and sex);
- body mass rate (BMR) – BMI multiplied by body surface area:

$$BMR = M^{1.425} \times 71.84/L^{1.275},$$

where: M – body mass (kg), L – length (cm).

The results were compared to standards for age and sex. Abnormal results were those below the low normal range;

- BF and FFM were assessed using 3 different methods:
 - measurement of skin folds using apparatus by Holtan Ltd., UK; for FFM the method modified by Ksiazek [4] was applied:
 - males below 11 years old:

$$LBM \text{ (lean body mass)} = \{100 - [(4.95/(1.169 - 0.0788 \times \log F) - 4.5) \times 100]\} \times MC/100$$

- males above 11 years old:

$$LBM = \{100 - [(4.95/(1.1533 - 0.0643 \times \log F) - 4.5) \times 100]\} \times MC/100$$

- females below 11 years old:

$$LBM = \{100 - [(4.95/(1.2063 - 0.0999 \times \log F) - 4.5) \times 100]\} \times MC/100$$

- females above 11 years old:

$$LBM = \{100 - [(4.95/(1.1369 - 0.0598 \times \log F) - 4.5) \times 100]\} \times MC/100,$$

where: MC – body mass (kg), F – sum of four skin folds (mm).

The values of BF and FFM were presented in the mean percentage for control group matched according to age and sex;

– BIA: whole-body BIA measurements were taken using two types of apparatus, MALTRON BF-905 (Maltron LTD, Essex, UK) and BODYSTAT 5000 (Bodystat Limited, Douglas, UK). All subjects were asked to lie in the supine position with legs apart (so as not touching at the thighs) and arms away from the body (so as not touching the torso). The measurement was taken in the morning on an empty stomach with four surface electrodes placed on the right ankle and wrist. An alcohol swab was used to clean all electrode sites prior to measurement. Fat-free mass was assessed using the index of Houtkooper *et al.* [5]:

$$LBM = 0.58 \times L^2/R + 0.24 M + 2.69,$$

where: L – length (cm), R – impedance (ohms), M – body mass (kg);

– DEXA – X-rays of two different energies were used to scan the body, one of which was absorbed more strongly by fat than the other. A computer subtracted one image from the other, and the differences indicated the amount of fat relative to other tissues at each point. The sum over the entire image enabled calculation of the overall body composition. During the examination all subjects were asked to lie in the supine position. The amounts of BF and FFM were presented in the mean percentage for the control group matched according to age and sex.

Total body water percentage (TBW%) and amount of extracellular fluid using bioelectrical impedance (BIA)

During the examination all subjects were asked to lie in the supine position and spot electrodes were placed on the hands and bare feet. Electrolyte gel was applied first, and then a current of 50 kHz was introduced.

Laboratory tests

Laboratory tests were carried out to estimate the nutritional state of children and function of their livers. Each patient had a blood sample taken in the morning,

before breakfast, and the following markers were assessed: albumins, cholesterol, retinol (vitamin A), α -tocopherol (vitamin E), 25-hydroxycholecalciferol (25(OH)D₃), trace elements such as iron and zinc, total and conjugated bilirubin, INR, alanine aminotransferase activity and γ -glutamyl transpeptidase.

Statistical analysis

The analysis was done using StatsDirect Statistical Software, version 2, 2, 8 (StatsDirect Ltd., Cheshire, UK). All values in the text refer to mean \pm standard error of the mean (\pm SEM). The amounts of BF and FFM were not normally distributed so they were presented as a medians within the range. Between group comparisons were made using χ^2 test (Fisher-Freeman-Halton), as appropriate. The small number of groups (< 5) was the reason for choosing this test. Comparison between means was assessed by ANOVA test for data distributed normally. For data not distributed normally, comparisons were made with the Mann-Whitney *U*-test (when $p < 0.05$) or Kruskal-Wallis test (when appropriate). A value of $p < 0.05$ was accepted as statistically significant. Linear regression analysis was used to determine the changes in FFM and BF measured by different methods.

Results

Anthropometric data

Malnutrition, based on < 10th percentile, was detected in 54.5% of children with biliary cirrhosis, 44.4% with post-hepatic cirrhosis and 9% with portal vein obstruction, respectively. Malnutrition, based on BMI < 10th percentile (Figure 1) and Cole's index (Table I) was detected in 60% of children with biliary cirrhosis, 55.5% with post-hepatic cirrhosis and 45.5% with portal vein obstruction, respectively.

Fat-free mass and BF measured by different methods were comparable. Fat-free mass in children with biliary cirrhosis was lower than in control groups, but no statistically significant differences were found among the study groups. Body fat was decreased in all examined children, but in children with biliary cirrhosis was significantly lower than in control groups (BIA) and in

patient with post-hepatic cirrhosis or portal vein obstruction (DEXA). There was a high correlation ($r = 0.97$ for all groups) between FFM measured by BIA (Figure 2) and DEXA (Figure 3). The correlation between anthropometry and DEXA was slightly lower ($r = 0.88$ for biliary cirrhosis; $r = 0.95$ for post-hepatic cirrhosis or portal vein obstruction, respectively). For BF, the correlation between BIA (Figure 4) and DEXA (Figure 5) was lower ($r = 0.87$ for biliary and posthepatic cirrhosis; $r = 0.97$ for portal vein obstruction, respectively) and between anthropometry and DEXA significantly lower ($r = 0.69$ for biliary cirrhosis; 0.76 for post-hepatic cirrhosis and 0.87 for portal vein obstruction, respectively) than results for FFM.

Total body water percentage and amount of extracellular fluid using bioelectrical impedance

Total body water percentage was significantly higher in all study groups than in healthy children. No statistically significant differences were detected among the study groups. Results measured by the two different apparatus were comparable, with no statistically significant differences. The content of extracellular fluid was higher in children with biliary and post-hepatic cirrhosis than in control groups ($p < 0.05$). Additionally, the

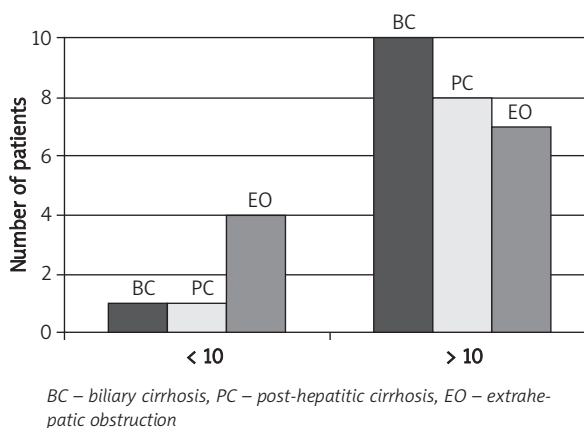


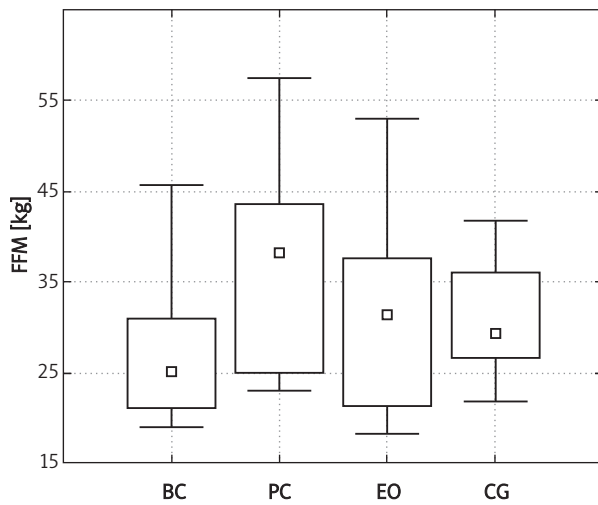
Fig. 1. Malnutrition based on BMI in study groups
Ryc. 1. Ocena niedożywienia na podstawie współczynnika BMI u analizowanych dzieci

Table I. Malnutrition based on Cole's index in study groups

Tabela I. Ocena niedożywienia na podstawie wskaźnika Cole'a u analizowanych dzieci

	Number of children with biliary cirrhosis	Number of children with post-hepatic cirrhosis	Number of children with portal vein obstruction
< 85%	3	2	3
> 85%	8	7	8

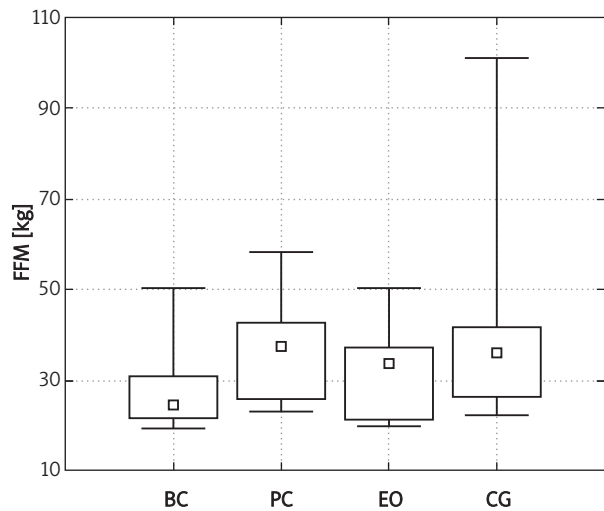
< 85% – malnutrition, > 85% – normal nutritional state



BC – biliary cirrhosis, PC – post-hepatic cirrhosis, EO – extrahepatic obstruction, CG – control group

Fig. 2. Comparison of FFM in study groups and control group measured by BIA method (Maltron apparatus)

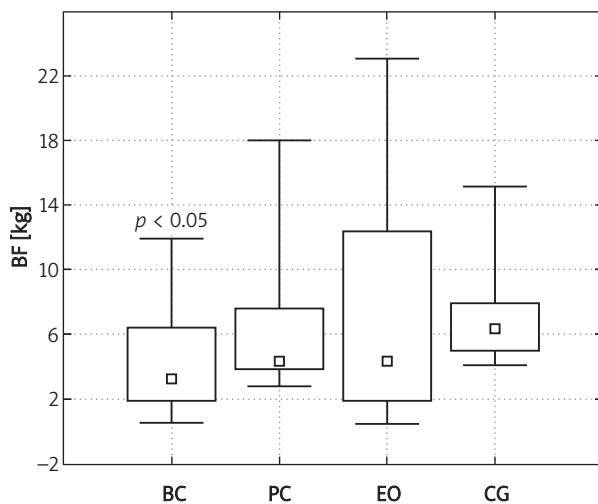
Ryc. 2. Zawartość BMC w porównaniu z zawartością w grupie kontrolnej mierzona metodą bioimpedancji elektrycznej (aparatur Maltron)



BC – biliary cirrhosis, PC – post-hepatic cirrhosis, EO – extrahepatic obstruction, CG – control group

Fig. 3. Comparison of FFM in study groups and control group measured by BIA method (Bodystat 5000 apparatus)

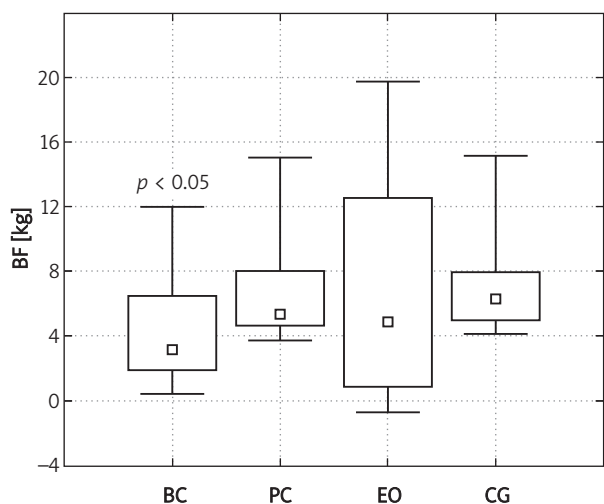
Ryc. 3. Zawartość BMC w porównaniu z zawartością w grupie kontrolnej mierzona metodą bioimpedancji elektrycznej (aparatur Bodystat 5000)



BC – biliary cirrhosis, PC – post-hepatic cirrhosis, EO – extrahepatic obstruction, CG – control group

Fig. 4. Comparison of BF in study groups and control group measured by BIA method (Maltron apparatus)

Ryc. 4. Zawartość masy tłuszczowej ciała w porównaniu z zawartością w grupie kontrolnej mierzona metodą bioimpedancji elektrycznej (aparatur Maltron)



BC – biliary cirrhosis, PC – post-hepatic cirrhosis, EO – extrahepatic obstruction, CG – control group

Fig. 5. Comparison of BF in study groups and control group measured by BIA method (Bodystat 5000 apparatus)

Ryc. 5. Zawartość masy tłuszczowej ciała w porównaniu z zawartością w grupie kontrolnej mierzona metodą bioimpedancji elektrycznej (aparatur Bodystat 5000)

results detected in patients with liver cirrhosis were significantly higher than in patients with portal vein obstruction. No statistically significant differences were found among children with biliary and post-hepatic cirrhosis.

The percentage of extracellular fluid in total body water was higher in children with biliary cirrhosis than in other groups ($p < 0.05$) (Figure 6). No statistically significant differences were found among other groups.

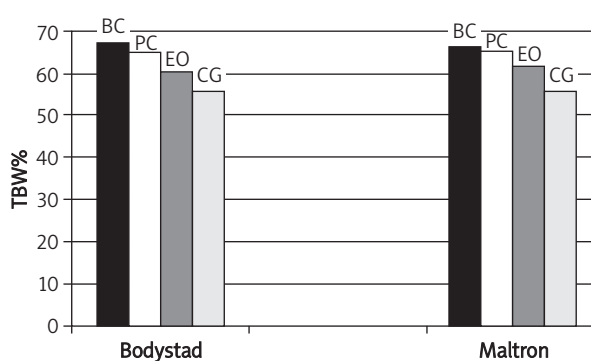
Laboratory data

Retinol (vitamin A) concentration was decreased in each group, and was the lowest in children with biliary cirrhosis. No correlation between the aminotransferase concentration and nutritional state was found. Table 1 shows the exact values of each laboratory parameter.

Discussion

Medical examination together with body mass and height measurement are still regarded as the most appropriate methods of assessing the patient's nutritional state. However, these parameters are adequate only in healthy people and patients with no disorders of body components such as oedema or ascites. Assessment of nutritional state in children is even more complicated, as their growth rate depends not only on developmental age, but also on higher nutrient and energy demands. Thus, the risk of malnutrition and its clinical consequences is more common and dangerous in paediatric patients, specially in those with liver disorders. Numerous studies have shown that children with liver disorders are particularly at risk of malnutrition because of their higher energy expenditure [6-9] and diminished intake. It is also known that improvement of the patient's nutritional state before liver transplantation will have a positive influence on the patient's post-transplant survival [10-12]. Therefore, it is of highest importance to apply accurate and reliable methods of nutritional state assessment in order to introduce adequate treatment such as enteral nutrition, as early as possible. Oedema, ascites, hepatomegaly and splenomegaly are often found in children with liver disorders, specially in those with cirrhosis and portal hypertension, which make proper examination difficult. Therefore, while making the diagnosis it is essential to apply extended, more objective methods such as assessment of body components, including TBW%. The aim of this study was to assess the nutritional state of children with liver disorders through different measurement methods.

Anthropometry such as height and weight analysis proved that the risk of malnutrition is higher in children with liver cirrhosis than in those with portal vein



BC – biliary cirrhosis, PC – post-hepatic cirrhosis, EO – extrahepatic obstruction, CG – control group

Fig. 6. Total body water percentage (TBW%) with reference to body mass in study groups and control group measured by both apparatus (Bodystat, Maltron)

Ryc. 6. Procentowa zawartość całkowitej wody w stosunku do masy ciała w organizmie badanych dzieci oraz w grupie kontrolnej

obstruction – distribution of percentile $< 10^{\text{th}}$ was found in 36.3% of children with biliary cirrhosis, 44.4% of post-hepatic cirrhosis and only in 18.2% of portal vein obstruction. Additionally, most examined patients had both height and weight deficiencies. However, BMI analysis revealed that only 1 patient with biliary cirrhosis, 1 with post-hepatic cirrhosis, and as many as 4 with portal vein obstruction had a decreased (< 10 percentile) BMI score. Those results proved that nutritional state assessment based on BMI only may lead to the incorrect conclusion that children with liver cirrhosis are not at risk of malnutrition. The proper BMI score in those patients is due to both height and weight deficiencies. Similar observations were published by Książyk [13], who also stated that BMI is not a sufficiently reliable method of nutritional state assessment in children. He proposed another indicator, WMC, that, apart from body height and weight, also includes body surface area and is very sensitive with reference to malnutrition (specially $< 10^{\text{th}}$ percentile). Cole's index detected more malnourished children with biliary cirrhosis than BMI but less than BMR, which proved that WMC is the most sensitive and is therefore recommended to diagnose malnutrition in children above 4 years old.

Estimation of body composition, most commonly the BF and FFM, is also useful in nutritional state assessment. Fat-free mass and BF remained stable in the study groups except in children with biliary cirrhosis, in whom both FFM and BF declined. Our observations are in concordance with those presented in similar studies [13-15]. Another acknowledged method of nutritional state

assessment is BIA, which enables the determination of both FFM and total body water (TBW) in subjects without significant fluid and electrolyte abnormalities [16, 17]. This method is popular owing to its ease of use, portability of the equipment and its relatively low cost compared to some of the other methods such as DEXA. In this study two types of apparatus, Maltron and Bodystat 5000, were used to estimate patients' body composition. Fat-free mass and BF measured by BIA, DEXA and anthropometric methods were comparable but TBW percentage and amount of extracellular fluid were significantly higher in children with liver cirrhosis (both biliary and post-hepatic) than in control groups. These results confirm Lehnert's [18] observations in adults – patients with liver cirrhosis are more predisposed to body water accumulation; thus assessment of nutritional state by primary methods only is difficult.

Comparison of FFM and BF measured by different methods proved that children with biliary cirrhosis are more exposed to malnutrition. However, FFM seems to be a less sensitive indicator of malnutrition due to its correlation with fluid disorders. DEXA correlates properly with both anthropometry and BIA. BIA can be applied in patients with ascites [18-20], in whom nutritional state is difficult to estimate. Similar observations were published by Kelly [11]; in his studies, > 60% of children with biliary cirrhosis had nutritional disorders before liver transplantation. Moukarzel *et al.* [21] analysed the death rate in patients after liver transplantation and he found that 80% of them were malnourished. This proved that nutritional state influences patients' survival time.

The analysis of laboratory parameters reflecting patients' nutritional state showed deficiencies of fat-soluble vitamin, as a result of its malabsorption. Vitamin A deficits were found in each study group, which confirmed the reports of other authors [14, 22, 23], but vitamin E concentration values in our patients were proper, in contrast to most published studies [14]. Constant management of children with portal hypertension, regular monitoring and adequate vitamin supplementation may explain these results. Patients with liver cirrhosis are treated with active vitamin D metabolite (Devisol, which is better absorbed than native vitamin D) as a standard therapeutic procedure. Thereby, we reported higher 25-hydroxycholecalciferol concentration in children with biliary cirrhosis than in those with portal vein obstruction. Our analyses lead to the conclusion that nutritional deficiency is more intense in patients with biliary than post-hepatic cirrhosis, which is associated with severe cholestasis and earlier activation of pathogenic factors.

Liver disorders lead to malnutrition, which is especially dangerous in children. Therefore, the assessment of nutritional state of patients with liver cirrhosis should be precise and objective so as to introduce proper treatment as early as possible. Anthropometry together with BIA and DEXA is very useful.

Conclusions

1. Children with portal hypertension, particularly with biliary liver cirrhosis, suffer from malnutrition, manifested by FFM decrease most frequently.
2. There is an increase of both TBW percentage and extracellular fluid content in children with liver cirrhosis (both biliary and post-hepatic).
3. The BIA method is useful in nutritional assessment in children with portal hypertension.
4. When comparing anthropometry, BMR has the advantage over BMI and Cole's index in nutritional assessment of children with portal hypertension.
5. There is a high correlation between BIA and DEXA in LBM and MT assessment in children with portal hypertension.
6. Decrease of vitamin A serum concentration is found to be a laboratory parameter of malnutrition in children with portal hypertension, particularly in those with biliary liver cirrhosis.
7. There is no proven correlation between the nutritional status and laboratory parameters of liver function in children with portal hypertension.

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