

The role of initial monitoring of routine biochemical nutritional markers in critically ill children[☆]

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Abstract

Aims: The objectives of this study were to determine whether abnormal values of routine laboratory parameters at admission predict outcome and changes in anthropometric parameters in critically ill children during intensive care unit (ICU) stay and to discuss the clinical implications of abnormalities.

Study design: This is a prospective descriptive study in a tertiary multidisciplinary pediatric ICU. Serum urea, albumin, triglycerides and magnesium were measured in samples obtained from 105 children (age, 7 days–16 years) within the first 24 h after their admission. The prevalences of abnormalities in these parameters as well as their possible association with outcome (length of stay, days on mechanical ventilation) and changes in nutritional status (changes in S.D. scores for weight, mid upper arm circumference and calf circumference) between admission and discharge were assessed.

Results: Prevalences of hypomagnesemia, hypertriglyceridemia, uremia and hypoalbuminemia were 20%, 25%, 30% and 52%, respectively, with no significant associations between the different disorders. Except for uremia, no significant association was found between abnormalities in biochemical parameters and changes in S.D. scores of anthropometric measurements. Children with uremia showed larger declines in S.D. scores for weight and arm circumference between admission and discharge than children without uremia did. Children with hypertriglyceridemia had longer ventilator dependence ($P < .01$) and length of stay ($P < .001$) than children with normal triglyceride levels upon admission had.

Conclusions: Abnormalities in routine nutritional laboratory parameters were frequently noted in critically ill children at admission. Detection of abnormalities was not predictive of changes in anthropometric parameters during ICU admission but can be important in individualizing nutritional support.

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1. Introduction

Malnutrition in the pediatric intensive care unit (ICU) population is a widely acknowledged problem that may intensify underlying illnesses, increase the risk of complications and affect growth and development [1,2]. Nutritional assessment upon admission to the ICU is necessary to identify children at risk and to guide nutritional support during ICU stay. The repertoire of routine laboratory

parameters includes several markers (e.g., albumin, urea, triglycerides, electrolytes) that can provide useful and easily obtainable information regarding nutritional status and requirements [3]. Abnormalities in these parameters reflect derangements in several metabolic pathways and may represent the severity of depletions occurring during critical illness. Previously, we have shown the nutritional status of children admitted to an ICU to deteriorate during admission [4]. By determining these biochemical parameters, we aim to identify specific derangements that may be related to the development of malnutrition in the ICU.

So far, data on the usefulness of an initial biochemical screening upon children's admission to the ICU as part of a

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comprehensive nutritional assessment including the implications for nutritional support and as a prognostic marker are lacking.

We set up this study to determine the prevalence of abnormalities in routinely available laboratory parameters related to nutritional status in critically ill children upon admission to the ICU and to investigate their usefulness in identifying children at risk of decline in nutritional status.

2. Materials and methods

The children described in this study participated in a prospective observational study on different aspects of nutritional assessment. The primary clinical results of this comprehensive study, encompassing all children admitted to the neonatal and pediatric ICU of our hospital in a 1-year period (2001) for at least 48 h, were published previously [4]. Patients older than 7 days and younger than 18 years were eligible for this part of the study. We excluded preterm neonates and children in whom treatment was withheld or withdrawn. The institutional review board of the Erasmus MC (Rotterdam, The Netherlands) approved the study protocol, and written (parental) informed consent was obtained before subjects entered the study (within the first 24 h after admission).

2.1. Clinical parameters

Clinical data collected included age, sex, surgical status, days on mechanical ventilation, length of ICU stay and mortality. The patients were classified in five diagnostic groups as shown in Table 1. Severity of illness upon admission was assessed by the Pediatric Risk of Mortality (PRISM) score [5].

2.2. Blood samples and measurements

Blood samples were taken for urea, albumin, triglycerides and magnesium within the first 24 h after the subjects' admission. Samples for all biochemical parameters could be obtained if an indwelling arterial line was present. Parameters could be missing for children in whom only a capillary blood puncture was possible. Exclusion criteria for the analysis of albumin included prior administration of hyperoncotic albumin solution (20%), fresh frozen plasma or pasteurized plasma solution. For the analysis of triglycerides, the administration of parenteral lipid emulsions was an exclusion criterion. Cutoff values conformed to the levels used by our clinical laboratory. Hypomagnesemia was defined as a serum magnesium level <0.76 mmol/L for neonates and <0.70 mmol/L for infants and children. Hypertriglyceridemia was defined as a serum triglyceride concentration >1.47 mmol/L. Uremia was defined as a serum urea level >4.2 mmol/L for neonates and >5.6 mmol/L for infants and children. Albumin concentrations <35 and <25 mmol/L were used as cutoff values for hypoalbuminemia in children and neonates, respectively. For continuous

Table 1
Patient characteristics (*N*=105)^a

Patient characteristics	
M/F	57:48 (54:46)
Age (years)	0.8 (8 days–15.5 years)
Age groups	
Term neonates	19 (18)
Older children (>30 days)	86 (82)
PRISM score	10 (0–31)
Length of stay ^b (days)	6 (2–35)
Mechanical ventilation	68 (65)
Duration ^b (days)	2 (0–35)
Surgery during ICU admission	45 (41)
Reason for ICU care	
Respiratory illness	37 (35)
Sepsis	16 (15)
Cardiac disease	21 (20)
Neurological/trauma	13 (12)
Other	18 (17)
Deceased during admission	7 (7)

^a Values are expressed as median (range) or as *n* (%).

^b Excluding the deceased children.

analysis of the levels of the different parameters, we adjusted for age by calculating the percentages of the lower limit (albumin, magnesium) or the percentages of the upper limit (urea). All levels were determined on a routine clinical chemistry analyzer (Hitachi 912, Roche Diagnostics, Almere, The Netherlands).

2.3. Anthropometric parameters

Weight, mid upper arm circumference (MUAC) and calf circumference (CC) were measured within 24 h after admission and at discharge from the ICU. Measurements were performed according to the methods described for Dutch reference values [6]. Intraobserver and interobserver studies performed prior to the study had shown good reproducibility of measurements with coefficients of variation <3% for MUAC and CC. Measurements of weight, MUAC and CC were converted to S.D. scores using recent Dutch reference standards [7]. The changes in S.D. scores for weight-for-age (WFA-SDS), MUAC (MUAC-SDS) and CC (CC-SDS) between admission and discharge were calculated.

2.4. Statistical analysis

Results are expressed as median (range) unless specified otherwise. The Mann–Whitney *U* test was used to compare levels of biochemical parameters between survivors and nonsurvivors and to compare PRISM scores, outcome variables (length of stay, length of mechanical ventilation, death) and changes in anthropometric measurements between children with and those without abnormalities in biochemical parameters. Spearman's correlation analysis was used to examine relationships between individual biochemical parameters and changes in S.D. scores of anthropometric values. χ^2 Tests (Pearson's, Fisher's Exact, Exact) were used to determine differences in the prevalence of abnormalities

between the different diagnostic groups and different age groups and relationships between the different abnormalities. A P value $< .05$ was considered statistically significant.

3. Results

A total of 105 children was included in the analyses. The children's characteristics are presented in Table 1. Seven of them died after a median stay in the pediatric ICU of 13.5 days (range, 2–83 days).

Table 2 shows the prevalence of hypomagnesemia, hypertriglyceridemia, uremia and hypoalbuminemia, together with the median values and range of parameters per age group. Fig. 1A–D shows scatter plots of the values for urea, albumin, triglycerides and magnesium for both age groups within the first 24 h after their admission. No significant association between abnormalities in individual parameters was found. The group of children with hypoalbuminemia consisted predominantly of children older than 30 days (25 of 27 children with hypoalbuminemia, $P < .01$). Significant differences for the prevalence of uremia were found between the five diagnostic groups ($P < .001$). Uremia was noted in 63% of children with sepsis and 60% of children with cardiac anomalies (9%, 25% and 13% for respiratory disease, trauma/neurological problems and other diagnoses, respectively).

3.1. Severity of illness and outcome

Children with uremia had a median PRISM score of 18 (0–31), which was significantly higher ($P < .001$) than that in children without uremia [9 (0–27)]. Children with

hypertriglyceridemia had a significantly higher PRISM score ($P < .05$), longer duration of mechanical ventilation ($P < .01$) and length of ICU stay ($P < .001$) than children without hypertriglyceridemia. No significant relationship was found for albumin, urea and magnesium levels and the number of days on mechanical ventilation or length of ICU stay. The seven children who died had a significantly higher median PRISM score ($P < .001$) and urea level ($P < .05$) upon admission than the survivors.

3.2. Anthropometric parameters

Median changes in WFA-SDS, MUAC-SDS and CC-SDS between admission and discharge were -0.15 S.D. (range, -1.6 – 2.06), -0.18 S.D. (range, -1.94 – 1.51) and -0.15 S.D. (range, -1.78 – 1.81), respectively. The urea level was significantly negatively correlated to the change in MUAC-SDS between admission and discharge ($r_s = -0.28$, $P = .013$). Furthermore, the children with uremia showed larger declines in WFA-SDS and MUAC-SDS between admission and discharge than children without uremia (median change in WFA-SDS: -0.51 vs. -0.04 SD, $P < .05$; median change in MUAC-SDS: -0.70 vs. -0.12 , $P < .001$). No relationship was found between abnormalities of the other biochemical parameters upon admission and changes in nutritional anthropometric parameters from admission to discharge.

4. Discussion

To minimize the deterioration of children's nutritional status during ICU admission, it would be helpful if those at risk could be identified at admission so that nutritional care could be tailored to their (individual) needs. Routine laboratory parameters may possibly serve as easily obtainable indicators [3].

In the present study, we found significant numbers of abnormalities in biochemical parameters routinely used for the initial screening of pediatric ICU patients. Previous studies in critically ill adults and children also found considerable proportions of abnormal levels of albumin, urea and magnesium upon admission [8–13]. To our knowledge, abnormalities in fasting triglyceride levels have not been reported before in children. So far, determination of serum triglycerides only served to check for parenteral nutrition-associated hypertriglyceridemia and to monitor the safety of parenteral fat administration [14–16]. Studies on critically ill adults have demonstrated that plasma triglyceride concentrations may increase, remain unchanged or decrease in different types of acute conditions [17,18]. Levels depend on the efficacy of mechanisms removing VLDL triglycerides (i.e., lipoprotein lipase-mediated lipolysis and tissue uptake of remnant particles). In many acute situations (trauma, surgery), these mechanisms are not impaired and triglyceride levels will be normal or low. In situations with high levels of the endotoxin lipopolysaccharide as in severe sepsis, the activity of lipoprotein lipase is

Table 2
Median level of biochemical parameters within the first 24 h after admission and prevalence of abnormal values

	<i>n</i>	Concentrations within first 24 h in the ICU ^a	Normal reference	Prevalence of abnormal values ^b (%)
Magnesium (mmol/L)	76	0.81 (0.40–1.21)		15 (20)
Neonates (0–30 days)	12	0.81 (0.67–0.99)	0.76–1.17	
Older children (>30 days)	64	0.81 (0.40–1.21)	0.70–0.95	
Albumin (g/L)	52	32 (20–49)		27 (52)
Neonates (0–30 days)	14	32 (20–35)	25–30	
Older children (>30 days)	38	32 (20–49)	35–50	
Urea (mmol/L)	99	3.8 (0.9–24)		30 (30)
Neonates (0–30 days)	17	3.4 (1.0–11.2)	1.7–4.2	
Older children (>30 days)	82	3.9 (0.9–24)	2.6–5.6	
Triglycerides (mmol/L)	55	0.94 (0.14–2.51)	<1.47	14 (25)

^a Values are expressed as median (range).

^b Rows correspond to hypomagnesemia, hypoalbuminemia, uremia and hypertriglyceridemia, respectively.

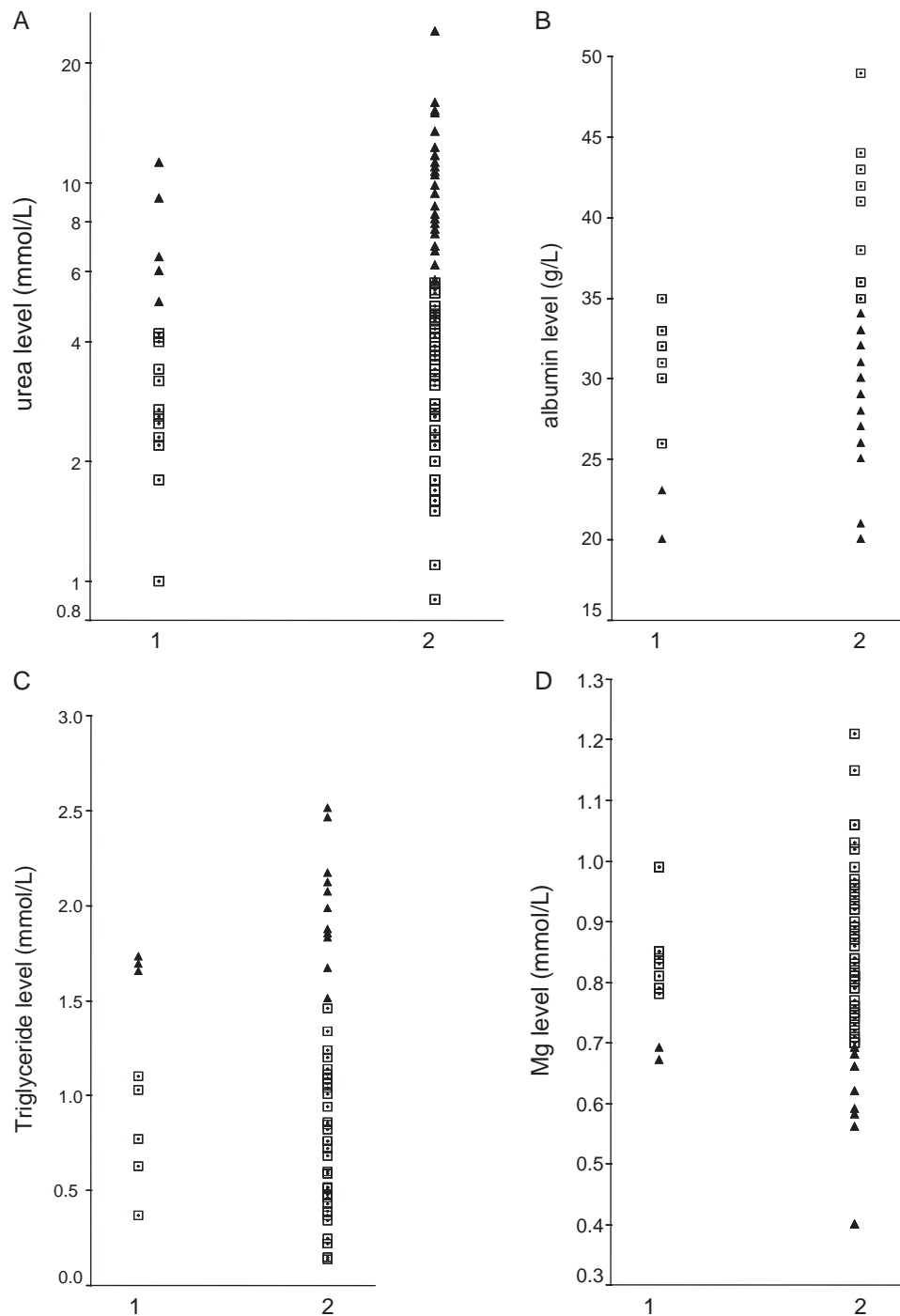


Fig. 1. Scatter plots for levels of urea (A), albumin (B), triglycerides (C) and magnesium (D) for the two age groups — term neonates (1) and older children (2) — indicating abnormalities (triangles).

depressed and triglyceride disposal is impeded, resulting in substantial elevations in plasma triglycerides. The high prevalence of elevated triglyceride concentrations found in our study in contrast to adult studies might be a result of a different acute stress response and modification of the hormonal milieu [19].

With regard to the clinical consequences of the abnormal levels, it is obvious that low levels of albumin and

magnesium will be treated. It is questionable, however, whether high levels of urea and triglycerides upon admission to the ICU will modify nutritional support strategies. Is it necessary to withhold fat emulsions in children who already have a high serum triglyceride level within the first 24 h after admission? No study has looked into this issue, but it can be speculated that adding fat to the diet will not benefit children who cannot metabolize fat.

Serum urea levels can indicate the degree of catabolic stress and level of protein breakdown associated with illness, surgery or trauma [3]. In this study, we demonstrated that children with high urea levels upon admission had larger declines in S.D. scores for anthropometric parameters during admission than children with low urea levels upon admission, indicating loss of muscle mass. In practice, however, high urea levels may also be caused by impaired renal function, dehydration, polyuria or severe sweating upon admission. High urea levels will therefore obviously affect fluid management; however, because high levels may reflect protein breakdown, extra attention should also be given to the energy intake and especially the protein intake of children.

Furthermore, several other metabolic parameters that may not be measured easily in plasma will show high prevalences of abnormalities as well. For example, hypomagnesemia is strongly associated with hypokalemia and hypocalcemia [20–23] and low levels of phosphorus, selenium, zinc and manganese are also commonly found in critical illnesses [24]. It might be postulated that combinations of those unidentified and untreated deficiencies may delay recovery because they all play key roles in many of the metabolic processes that promote recovery from critical illness [24]. While this study revealed hypertriglyceridemia to be related with poorer outcome variables, previous studies in critically ill adults and children revealed associations between hypoalbuminemia [8,9,25] and hypomagnesemia [22,26–28], with increased likelihood of mortality, morbidity, prolonged ventilator dependence and prolonged ICU and hospital stay. Perhaps the fact that most children in our study were treated (data not shown) explains why we did not find any association between hypoalbuminemia or hypomagnesemia and outcome variables. The clinical significance of the association between hypertriglyceridemia and length of stay and duration of mechanical ventilation still has to be determined. Yet our data suggest that it may just reflect a higher severity of illness, a finding that was also observed in adult ICU patients [18].

The limitations of our study should be noted. First, although it represents an analysis of prospectively collected data, the fact that our study protocol did not allow us to obtain all biochemical parameters in all children might have led to selection bias with overrepresentation of the more severely ill children. As they usually have indwelling arterial lines, blood samples are easier to obtain from these children. Furthermore, although all were severely ill, the heterogeneity of our study population might explain the lack of associations. Some of the parameters studied could well be useful in more specific diagnostic groups. Second, we did not correct for possible other factors, such as use of medication, acidosis and gastrointestinal losses, which may influence the levels of the different biochemical parameters. These factors, together with the timing of the blood sampling, can influence the sensitivity and specificity of the laboratory tests as alterations in levels of the measured

biochemical parameters can occur quickly within the first 24 h after admission, when fluid shifts take place.

In conclusion, this study showed that the levels of the routinely available biochemical parameters urea, albumin, triglycerides and magnesium are frequently abnormal. These abnormalities, although not associated with changes in anthropometric parameters during admission, have important implications for providing individualized and optimal nutritional support during ICU stay and should therefore be performed.

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