Nutrition and Metabolism Research Paper Sessions

Session Title
Critical Care and Other Critical Health Issues

3069630 - Application of Nutrition Risk in Critically ill (NUTRIC) score for nutritional risk assessment and prognosis prediction in neurological critically ill patients: a prospective observational study

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Purpose: Critically ill patients in neurological intensive care unit (NICU) are susceptible to nutritional risk. High nutritional risk in NICU patients is associated with adverse clinical outcomes. Thus nutritional risk assessment must be done on all NICU patients. Nutrition Risk in Critically ill (NUTRIC) score is an ICU-specific nutrition risk assessment tool which combines both patients' acute ill condition and nutrition status. However, since its recent propose, the application of NUTRIC score in NICU patients hasn't been reported yet. This study aims at investigating the value of NUTRIC score system in nutritional risk assessment and prognosis prediction in neurological critically ill patients.
Methods: This prospective observational study consecutively enrolled in 140 neurological critically ill patients who were admitted into our NICU. Demographic data, height, body weight, main diagnosis, complications, nutritional support pattern, hospital infection, vasopressor administration, renal replacement therapy, mechanical ventilation, length of NICU stay, length of hospital stay, NICU mortality and 28-day mortality were collected. Nutrition risk screening 2002 (NRS 2002), NUTRIC score and modified NUTRIC (mNUTRIC, without IL-6) score were applied for all enrolled patients at NICU admission.
Results: NICU patients exhibited high nutritional risk. By NUTRIC scoring, high nutritional risk (NUTRIC score≥6) existed in 84.3% of NICU patients, while low nutritional risk (NUTRIC score＜6) existed in 15.7% patients. By mNUTRIC scoring, high nutritional risk (mNUTRIC score≥5) existed in 71.4% of NICU patients, while low nutritional risk (mNUTRIC score＜5) existed in 28.6% patients. Through multivariate analysis, age≥60 years, hospital infection, mechanical ventilation, and high nutritional risk (mNUTRIC score≥5) were identified to be independent risk factors for 28-day death. In the subgroup of patients with NICU stay≥1 week, mechanical ventilation and high nutritional risk (mNUTRIC score≥5) were independent risk factors for 28-day death. While in the subgroup of patients with NICU stay≥2 weeks, only high nutritional risk (mNUTRIC score≥5) remained significant as an independent risk factor for 28-day

death. According to mNUTRIC score, high nutritional risk group (mNUTRIC score≥5) exhibited significant higher incidences of lung infection, hospital infection, organ dysfunction, vasopressor administration and mechanical ventilation, as well as significantly increased NICU mortality and 28-day mortality than low nutritional risk group (mNUTRIC score＜5). NUTRIC score predicted 28-day mortality with area under the curve (AUC) of 0.857 (95% confidence interval [CI] 0.786-0.928). While mNUTRIC score predicted 28-day mortality with AUC of 0.856 (95%CI 0.786-0.927).
Conclusions: The mNUTRIC score is not only a useful tool for nutritional risk assessment, but also a good prediction tool for 28-day death for neurological critically ill patients in NICU. Furthermore, as the prolongation of NICU stay, the prognosis predictive value of mNUTRIC score could be more meaningful than other measurements. Therefore, mNUTRIC score is a recommended tool for nutritional risk assessment and prognosis prediction in NICU.

Financial support received from: None.

3077809 - Nurse-driven Bedside Blind Placement of Post-pyloric Feeding Tube in the PICU is Feasible and Safe

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Purpose: Enteral nutrition (EN) delivery has been associated with improved clinical outcomes in critically ill children. Enteral nutrition can be delivered via the gastric or post-pyloric (PP) route. Although the PP route has been associated with lower incidence of EN intolerance and aspiration, expertise and resources are required for PP tube placement with potential for adverse events. We aimed to describe the results of a nurse-driven bedside PP tube placement program in a pediatric multidisciplinary intensive care unit (PICU).
Methods: In a single-center retrospective study, we reviewed the electronic medical record of all patients admitted for a minimum of 48 hours to two multidisciplinary PICUs within our institution in whom PP tube placement was attempted. Demographics, clinical indication for PP tube placement, variables associated with PP tube placement, and adverse events were extracted. Data are presented as median (interquartile range) and frequency (percentage).
Results: Ninety-nine patients underwent a PP tube placement; median age was 4.06 years (0.52, 14.88) and 65/99 (65.7%) were male. The indication for PP tube placement was recorded in 65 patients, 20 of which had more than one indication. The most common reasons for PP tube placement were EN intolerance including gastrointestinal (GI) dysmotility (33/65, 50.8%), risk for or known aspiration (32/65, 49.2%), and non-invasive ventilation (22/65, 33.8%). Initial PP tube placement attempt was made by a bedside registered nurse (58/99, 58.6%) or clinical nurse specialist (34/99, 34.3%) using a blind-placement technique in 92/99 (92.9%). In the remaining 7/99 (7%) patients PP tube placement was achieved in fluoroscopy/ interventional radiology (IR) (5/99, 5%) or by surgical direct palpation (2/99, 2%) by a physician. PP tube was successfully placed at the bedside in 85/99 (85%) of patients, with a median number of 1 (1,2) attempts and 1 (1,2) confirmatory radiographs. Initial PP tube placement was not successful in 14/99 (14.1%) patients. For 9/14 (64%) of this sub-cohort an alternative technique was attempted. The median number of bedside attempts and radiographs prior to pursuing an alternative PP placement technique were 2 (1,4) and 2 (1,4), respectively. Alternative techniques included placement under fluoroscopy/ IR (6) and gastrostomy to gastrostomy-jejunostomy tube conversion (2). For 7 patients in this sub-cohort the alternative technique resulted in successful placement, however median time from first attempt to successful placement was 192 hours (71, 558). GI anatomical locations for the PP tube tip on radiograph for patients with successful PP tube placement, irrespective of technique, were the distal duodenum (47/92, 51.5%), the proximal duodenum (31/92, 33.7%) and the jejunum (14/92, 15.2%). No alternative PP tube placement was attempted for 6/99 (6%) patients. Metoclopramide was administered

for PP tube placement in 67/99 (67.7%) patients. Metoclopramide did not improve the odds of successful PP tube placement by Fisher's exact test (OR 0.375, 95% CI 0.08-1.78, p0.335). GI bleeding was noted in 4/99 (4%) and bradycardia in 1/99 (1%) patients. Tube displacement was noted in 24/92 (26.1%) and tube blockage requiring exchange in 5/92 (5.4%) patients.
Conclusions: Successful PP tube placement by the blind-bedside technique is feasible and safe for a majority of PICU patients. Early consideration of alternative placement techniques for the unsuccessful bedside placement is important to reduce delays in placement and EN delivery. Further studies examining the indications for PP feeding, and to explore the difference in clinical outcomes between gastric and PP EN in the PICU are needed.

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BEST OF ASPEN – CRITICAL CARE TOPICS
ABSTRACT OF DISTINCTION

3045614 - Early Enteral Nutrition in Septic Shock: A Randomized Controlled Pilot Study

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Purpose: Enteral nutrition aims to maintain enterocyte mass and function, preserve gut immune function, and prevent complications. Impaired gut function is often observed in septic shock. The optimal dose, timing, and impact of early EN in septic shock are not well defined. We hypothesized early trophic EN, as compared to no EN, in septic shock would be tolerated without complications and increase ICU-free days.
Methods: We conducted a single-center, randomized controlled pilot trial (RCT) comparing early trophic EN to 'no EN' in mechanically ventilated medical intensive care unit (ICU) adults (>18 years old) with septic shock. In a concealed fashion, enrolled patients were randomized within 24 hours of intubation to receive early EN, defined as 20 mL/hour of iso-osmotic formula, or 'no EN.' In the early EN group, 20 mL/hour was continued until vasopressor(s) was discontinued for at least 3 hours or 48 hours after enrollment, at which point EN was advanced to prescribed goal. In the 'no EN' group, EN was commenced when vasopressor(s) was discontinued for at least 3 hours or 48 hours after enrollment, at which point EN was advanced to prescribed goal. The pilot study assessed feasibility in delivering EN without complications and ICU-free days. Other outcomes included hospital mortality and ventilator-free days (VFD). ICU free days and VFD were compared between the groups using the Wilcoxon rank-sum test. All analyses were on a modified intention-to-treat basis.
Results: Between January 27, 2014 and November 1, 2017, we randomized 31 patients. Fifteen were randomized to receive early EN and 16 to 'no EN.' Protocol violation occurred in one patient. Thirty were included in the per protocol analysis. Median age in early EN and 'no EN' groups was 56 and 64 years, respectively. Median SOFA score in early trophic EN and 'no EN' groups was 12 and 11, respectively. Median APACHE II score was 23 in both groups. Twenty percent in both groups had severe malnutrition. While on vasopressors, the early EN group received total median 384 kcal and the 'no EN' group received a median of zero kcal. Twenty percent of early EN had a vomiting episode over the first 7 days, as compared to 60% in the 'no EN' group (p=0.025). No patient had non-occlusive mesenteric ischemia, non-occlusive bowel necrosis, bowel obstruction, or ileus. Candida was isolated in cultures from 6/15 patients in the 'no EN' group and 1/15 from the early EN group (p=0.08). The early EN had median 25 ICU-free days, as compared to 12 in the 'no EN' group (p=0.014). Early EN had median 25 VFD, as compared to 12 in 'no EN' group (p=0.009). Two (13%) in the early EN, as compared to 5 (33%) in 'no EN' died during hospitalization (p=0.39).

Conclusions: Our pilot RCT demonstrates the feasibility of evaluating two different feeding strategies in patients with septic shock and shows early EN, as compared to no EN, was well tolerated. Ours is the first RCT comparing early EN to 'no EN' in septic shock and suggests non-nutritional benefits of early trophic EN. A larger multi-center trial is warranted to confirm the observed clinical benefits seen in this trial.

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ABSTRACT OF DISTINCTION

3078132 - A commensal anti-inflammatory bacterium promotes weight gain and survival in septic mice

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Purpose: Intestinal epithelial cells maintain intimate relationships with microbial communities that influence diverse aspects of physiology and homeostasis. These microbial communities, termed the intestinal microbiota, modulate nutrient metabolism and absorption and edify the host immune system. Abnormal microbiota assemblies and loss of beneficial communities that support healthy nutrient metabolism and absorption are implicated in several human diseases and occurs early in critical illness. Indeed, our group has shown critical illness is associated with significant and rapid change to the microbiota, including a significant loss of the beneficial bacterium *Faecalibacterium prausnitzii*. This bacterium is similarly lost in microbiota assemblies from inflammatory bowel disease (IBD) patients. It is known that supplying this bacterium reduces intestinal inflammation in experimental models of IBD; further, it is associated with remission of active IBD in patients. However, unlike IBD, it remains unknown if loss of *F. prausnitzii* or other beneficial microorganisms contribute to critical illness. Similarly, the bacterium *Lactobacillus plantarum* has recently been shown to promote survival and reduce occurrence of neonatal sepsis in rural India; however, the mechanisms of how this bacterium and other *Lactobacilli* improve survival in sepsis remains unknown.
Methods: Male mice received daily gavages of 10^9 colony forming units (CFUs) of *F. prausnitzii* or water for 1 week. After 1 week of pretreatment, the mice were anesthetized and their cecum was ligated ~0.5 cm distal the ileal-cecal valve and the ligated tissue was punctured with a 23G needle. The surgical wound was closed and the mouse was allowed to recover from anesthesia. Mice were monitored and weighed daily following the cecal-ligation and puncture (CLP) surgery. To identify mechanisms of how *F. prausnitzii*, *L. plantarum* and *Lactobascillus Rhamnosus GG* (*LGG*) promote survival in sepsis, we performed *in vitro* growth assays to test if biproducts of their metabolism/growth in liquid culture suppress the growth of a sepsis causing bacterium: *Staphylococcus aureus*.
Results: We found that *F. prausnitzii* (but not *L. plantarum*) supplementation promotes boh survival and weight gain in septic mice. Surprisingly, we found that daily doses of *F. prausnitzii* does not reduce bacteremia 24 hours following induction of sepsis; these results suggest that *F. prausnitzii* improves survival in septic mice via a potentially novel mechanism which may not involve improving intestinal barrier function as has been observed with other probiotic strains we have studied (*LGG*). These findings are similar to results we have previously obtained in this model with *Bifidobacterium longum* which also improves survival in sepsis without improving bacteremia. We found that conditioned media from *F. prausnitzii*, *L. plantarum* and *LGG* significantly suppressed *S. aureus* growth; our data indicate these bacteria produce a bactericidal or bacteriostatic factor that inhibit *S. aureus* growth. *L. plantarum* and *LGG* acidify culture media by generating lactic acid; Interestingly, *F. prausnitzii* conditioned media remains at the same pH as *S. aureus* conditioned media.
Conclusions: Cecal-ligation and puncture results in substantial weight loss in both control and *F. prausnitzii* treated mice. However, *F. prausnitzii*-treated septic mice regain weight sooner and/or at a faster rate than water-treated septic mice. Further, biproducts of *F. prausnitzii* growth suppresses *S. aureus* growth in our in vitro system. The capacity of *F. prausnitzii* to inhibit pathogen growth and improve host weight gain may contribute to the protective mechanisms of *F. prausnitzii* on critically-ill mice.

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INTERNATIONAL ABSTRACT OF DISTINCTION

3069867 - Persistent inflammation, immunosuppression and catabolism syndrome (PICS): a proposal for definition in critically ill children

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Purpose: Persistent inflammation, immunosuppression and catabolism syndrome (PICS) has been described in critically ill adults and may contribute to unfavorable outcomes. However, PICS has not been evaluated in critically ill children. This study aimed to define and characterize PICS in critically ill children and to verify its association with clinical outcomes.
Methods: Prospective study conducted in a Pediatric Intensive Care Unit (PICU), with children aged between 1 month and 15 years admitted for at least 48 hours to medical and surgical PICU in the south of Brazil. Exclusion criteria were death within 72 hours of admission. Clinical, demographic, anthropometric, biochemical and nutritional therapy parameters were assessed. Duration of mechanical ventilation, PICU and hospital length of stay (LOS) and overall-mortality were recorded in the patient chart. Based on the model proposed by adults, we selected several variables to propose different models to identify patients with PICS. Logistic and Cox regression were applied, and the results were expressed, respectively, as odds ratio (OR) and hazard ratio (HR). P-value <0.05 was considered significant.
Results: There were included 201 children (median age 27 months, 63% male). The mortality rate was 13%. Among the 47 surgical patients, 5 (10.64%) were neurosurgery, 10 (21.28%) were cardiac surgery and 32 (68.09%) were general surgery. Among the 6 PICS models proposed, only the model 1 (PICU LOS >14 days; C-reactive protein (CRP) >10.0 mg/L; lymphocytes <25%; reduction of z-score mid-upper arm circumference) was associated with mortality (Table 1). Based on model 1, the prevalence of PICS was 3.5%. The pediatric index of mortality (PIM 2) (p=0.156), and diagnostic (p=0.208) were not different between patients with and without PICS, while the duration of vasoactive drugs and antibiotics, in days, were higher in patients with PICS (p<0.001). After adjustment for PIM 2, patients with PICS had lower chance of an earlier PICU discharge (HR 0.28; 95% CI 0.10; 0.76; p=0.012), hospital discharge (HR 0.28; 95% CI 0.10; 0.77; p=0.013) and extubation (HR 0.28; 95% CI 0.10; 0.78; p=0.015). Similar results were found for a subset of critically ill children that required mechanical ventilation for more than 48 hours (Table 2).
Conclusions: The definition of PICS proposed in this study was associated with clinical outcomes in critically ill children. More studies are needed to properly define and validate PICS for this population.

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Table 1 – Different models for Persistent inflammation, immunosuppression, and catabolism syndrome (PICS) and the association with overall-mortality.

Models	PICS n (%)	Crude		Adjusted [a]	
		OR (95% CI)	p-value	OR (95% CI)	p-value

Model 1 PICU LOS >14 days CRP >10.0 mg/L lymphocytes <25% reduction of MUAC/A z-score after 14 days	7 (3.48)	5.58 (1.17; 26.51)	**0.031**	5.09 (1.06; 24.58)	**0.043**
Model 2 PICU LOS >14 days CRP >10.0 mg/L nosocomial infection albumin <3.0 g/dL	7 (3.48)	2.83 (0.52; 15.43)	0.228	3.30 (0.60; 18.26)	0.172
Model 3 PICU LOS >14 days CRP >10.0 mg/L lymphocytes <25% albumin <3.0 g/dL	5 (2.49)	4.78 (0.76; 30.07)	0.096	5.43 (0.85; 34.68)	0.073
Model 4 PICU LOS >14 days CRP >10.0 mg/L nosocomial infection reduction of MUAC/A z-score after 14 days	5 (2.49)	1.71 (0.18; 15.92)	0.637	1.47 (0.15; 14.07)	0.737
Model 5 PICU LOS >14 days CRP >10.0 mg/L nosocomial infection MUAC/A z-score <-2 at any time	3 (1.49)	3.46 (0.30; 39.57)	0.318	2.61 (0.22; 31.34)	0.450
Model 6 PICU LOS >14 days CRP >10.0 mg/L nosocomial infection reduction of MUAC/A z-score at any time	8 (3.85)	4.43 (0.99; 19.80)	0.051	4.17 (0.92; 18.86)	0.064

[a] adjusted for Pediatric Index of Mortality (PIM) 2 OR: odds ratio; PICU: Pediatric Intensive Care Unit; LOS: length of stay; CRP: C-reactive protein; BMI/A: body mass index-for-age; MUAC/A: mid upper arm circumference-for-age.

Table 2 - Cox Regression of clinical outcomes in critically ill children (n=201) and in a sample of critically ill children with mechanical ventilation (MV) >48 hours (n=146).

Variables	**PICS – model 1** [a]			
	Crude		**Adjusted** [b]	
	HR (95% CI)	**p-value**	**HR (95% CI)**	**p-value**
PICU LOS (days) (n=201)	0.26 (0.10; 0.71)	**0.009**	0.28 (0.10; 0.76)	**0.012**
Hospital LOS (days) (n=196)	0.27 (0.10; 0.73)	**0.010**	0.28 (0.10; 0.77)	**0.013**
Duration MV (days) (n=179)	0.27 (0.10; 0.74)	**0.011**	0.28 (0.10; 0.78)	**0.015**
MV >48 hours (n=146)				
PICU LOS (days) (n=146)	0.31 (0.11; 0.84)	**0.022**	0.33 (0.12; 0.90)	**0.031**

Hospital LOS (days) (n=142)	0.31 (0.11; 0.86)	**0.024**	0.33 (0.12; 0.91)	**0.033**
Duration MV (days) (n=146)	0.28 (0.10; 0.78)	**0.015**	0.30 (0.10; 0.82)	**0.019**

HR: Hazard ratio; PICU: Pediatric Intensive Care Unit; LOS: length of stay; MV: mechanical ventilation; CI95%: confidence interval 95%; [a] PICU LOS >14 days and C-reactive protein (CRP) >6.0 mg/dL and lymphocytes <25% and reduction of mid upper arm circumference-for-age z-score after 14 days; [b] Adjusted for Pediatric Index of Mortality 2

INTERNATIONAL ABSTRACT OF DISTINCTION

3069183 - Efficacy of thiamine, pyridoxine, and folic acid supplementation in critically ill patients requiring continuous renal replacement therapy: a retrospective study.

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Purpose: To evaluate the efficacy of the current micronutrient supplementation protocol at Emory University Hospital (EUH) in reducing the incidence of micronutrient deficiencies in critically ill patients requiring continuous renal replacement therapy (CRRT) versus previously published data.
Methods: Single-center, retrospective chart review of patients who received CRRT from March 1st 2014 through August 31st 2017 with a micronutrient supplementation protocol consisting of intravenous thiamine 100 mg, pyridoxine 200 mg, and folic acid 1 mg every 48 hours while on CRRT. Demographic data (age, gender, height, weight) and relevant treatments were obtained for each subject included in this study. In addition, micronutrient levels, date and time of CRRT initiation and discontinuation were recorded. Patients who received CRRT for <48 hours and/or did not have a micronutrient level drawn were excluded. The primary objective of the study is to evaluate the efficacy of the current thiamine, pyridoxine, and folic acid supplementation protocol on reducing the incidence of thiamine, pyridoxine and folic acid deficiencies in critically ill patients requiring CRRT versus previously published data at EUH. Other objectives included the assessment of all micronutrient levels in relation to the initiation and/or discontinuation of CRRT, hospital length of stay, and hospital mortality. The study was approved by the institutional review board of EUH.
Results: A total of 259 patients were included with a mean age of 54 years (range,18-94). The most common reasons for ICU admission were respiratory failure (25%), postoperation (18%), end-stage liver disease (15%), sepsis (13%), cardiogenic shock (8%), renal failure (6%), and heart failure (4%). A total of 34% of study subjects had end-stage renal disease (ESRD) prior to ICU admission. Past medical history for included patients was significant for cirrhosis (21%), cancer (16%), alcohol abuse (14%), gastroesophageal reflux disease (7%), enterocutaneous fistula (3%), and Crohn's disease (1%).The average number of days that patients required CRRT was 10.1 days and hospital mortality averaged 50%. Twenty-four patients received parenteral nutrition during CRRT therapy.

Thiamine deficiency was documented in 1% of patients as compared to previously published data. (Table-1) Pyridoxine and folic acid deficiencies were documented in 39 % and 9 % of patients and did not change significantly when compared to previously published data. Copper and carnitine showed significant low levels pre-CRRT, during CRRT, and post-CRRT. All levels obtained during CRRT were deficient of 25-hydloxycholecalciferol. (Table-2) Vitamin C was significantly deficient during CRRT. Eighty-seven percent of patients were vitamin C deficient during CRRT with 42% who had undetectable levels (<5 mcmol/L).
Conclusions: Current micronutrient supplementation protocol with CRRT reduced the incidence of patients with thiamine, pyridoxine and folate deficiencies. The incidence of vitamin C and copper deficiencies remains high and may warrant modification to the current protocol to include vitamin C and copper. The need for a prospective study to delineate the optimal supplementation regimen is warranted.

Financial support received from: N/A

Micronutrient Deficiencies Identified

Micronutrient	Thiamine			Pyridoxine			Folate			Copper			Ceruloplasmin			Free Carnitine			Total Carnitine			Zinc			Selenium		
Reference range	70-180 nmol/L			20-125 nmol/L			≥ 5.9 ng/ml			80-155 mcg/dl			21-53 mg/dl			20-60 mcmol/L			34-86 mcmol/L			60-120 mcg/dl			70-190 mcg/dl		
Time of micronutrient level	Pre-CRRT	During CRRT	Post-CRRT	Pre-CRRT	During CRRT	Post-CRRT	Pre-CRRT	During CRRT	Post-CRRT	Pre-CRRT	During CRRT	Post-CRRT	Pre-CRRT	During CRRT	Post-CRRT	Pre-CRRT	During CRRT	Post-CRRT	Pre-CRRT	During CRRT	Post-CRRT	Pre-CRRT	During CRRT	Post-CRRT	Pre-CRRT	During CRRT	Post-CRRT
Total number of levels	32	84	19	31	98	39	22	67	28	50	147	51	67	116	41	10	54	14	9	54	13	29	79	37	17	63	17
Number of patients with micronutrient deficiency	15	1	2	14	38	19	1	6	1	24	68	25	26	26	12	2	14	4	1	11	2	15	16	8	3	7	3
Percentage of patients with micronutrient deficiency	47%	<1%	11%	45%	39	49%	5%	9%	4%	48%	46%	49%	39%	22%	29%	20%	26%	28%	11%	20%	15%	52%	20%	22%	18%	11%	18%

Micronutrient Deficiencies Identified (continued)

Micronutrient	Vitamin C	25-hydroxycholecalciferol

Reference range	23-114 mcmol/L			29.9-74 ng/ml		
Time of micronutrient level	Pre-CRRT	During CRRT	Post-CRRT	Pre-CRRT	During CRRT	Post-CRRT
Total number of levels	23	113	51	28	16	23
Number of patients with micronutrient deficiency	18	98	39	26	16	21
Percentage of patients with micronutrient deficiency	78%	87%	76%	93%	100%	91%
Number of patients with undetectable Vitamin C level (< 5 mcmol/L), (%)	6, (26%)	48, (42%)	17, (33%)			