GLOBAL VARIATION OF NUTRITIONAL STATUS IN CHILDREN UNDERGOING CHRONIC PERITONEAL DIALYSIS

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Global Variation of Nutritional Status in Children Undergoing Chronic Peritoneal Dialysis: A Longitudinal Study of the International Pediatric Peritoneal Dialysis Network


While children approaching end-stage kidney disease (ESKD) are considered at risk of uremic anorexia and underweight they are also exposed to the global obesity epidemic. We sought to investigate the variation of nutritional status in children undergoing chronic peritoneal dialysis (CPD) around the globe. The distribution and course of body mass index (BMI) standard deviation score over time was examined prospectively in 1001 children and adolescents from 35 countries starting CPD who were followed in the International Pediatric PD Network (IPPPN) Registry. The overall prevalence of underweight, and
CONTENT OUTLINE

- International Pediatric Dialysis Network (IPDN)
- Introduction & Background
- Objectives
- Methods
- Results
- Conclusions
INTERNATIONAL PEDIATRIC DIALYSIS NETWORK (IPDN)
The IPDN is a global consortium of pediatric nephrology centers dedicated to the care of children on chronic dialysis. The IPDN aims to:

- Improve the quality of pediatric dialysis care worldwide
- Collect basic information regarding pediatric dialysis practices and outcomes
- Provide useful tools and management algorithms for daily dialysis practice
- Provide global benchmarking of pediatric dialysis outcomes
- Perform prospective observational studies on important clinical issues in pediatric dialysis
IPDN

- IPDN entertains two registries:
  - The IPPN registry for children on chronic peritoneal dialysis
  - The IPHN registry for children on hemodialysis

- To date:
  - 3729 patients have been enrolled in the IPPN Registry at 128 contributing centers in 43 countries
  - 957 patients have been enrolled in the IPHN Registry at 85 contributing centers in 36 countries
Network Participants

- 000-Testcenter, 000 - Testcenter
- Aarhus, Aarhus University Hospital
- Abu Dhabi, Sheikh Khalifa Medical City, Department of Pediatrics
- Adana, Cukurova University, Faculty of Medicine, Department of Pediatric Nephrology
- Al Ain, Tawam Hospital
- Albuquerque, University of New Mexico
- Alexandria, Damascus Hospital
- Amsterdam, Academic Medical Center
- Ankara, Hacettepe University
- Ankara, Ankara University School of Medicine
- Ankara, Gaziantep University Hospital
- Ann Arbor, MI, University of Michigan Mott Hospital
- Athens, A & P Kyrkiou Children's Hospital
- Atlanta, Children's Healthcare Pediatric Dialysis Unit
- Auckland, Starship Children's Hospital
- Bahia Blanca, Unidad de Nefrologia Pediatrica del Hospital Interzonal General
- Baltimore, Johns Hopkins Hospital
- Bangalore, St Johns Medical College Hospital, Childrens Kidney Care Center
- Bangalore, Rainbow Children's Hospital, Marathahalli
- Bangkok, King Chulalongkorn Memorial Hospital
- Baracaldo, Hospital de Cruces
- Barcelona, Hospital Universitario Materno-Infantil Vall d’Hebron
- Barcelona, Hospital Sant Joan de Deu
- Bari, Pediatric Hospital Giovanni XXIII
- Beer Sheva, Soroka Medical Center
- Cuzco, Hospital Infantil Federico Gomez
- Cusco, Pediatric Hospital Medical Center SXXI
- Dallas, Children's Medical Center Dallas
- David, Chiriqui, Hospital materno infantil Jose Domingo De Obaldia
- Dubai, Dubai Hospital
- Dubai, Al Jalila Children's Speciality Hospital
- Dublin, Temple Street Children's University Hospital
- Durham, Duke University
Center Details

Dubai, Dubai Hospital

Head of unit: Dr. Loai Akram Ouda Eid
IPPN Lead investigator: Dr. Loai Eid

Address:
PO Box 4545
Dubai
United Arab Emirates

Phone: +9742195335
Fax:

Webpage:

Renal replacement services offered by center
CAPD (Continuous Ambulatory Peritoneal Dialysis)
APD (Automated Peritoneal Dialysis)
Hemodialysis
Hemofiltration/Hemodiafiltration
Plasmapheresis/Immunoabsorption
Continuous Extracorporeal Techniques

Center statistics
Estimated catchment in million general population: 2
Number of CKD patients currently in predialysis care: 10
Number of ESRD patients currently on chronic PD: 5
Number of ESRD patients currently on chronic hemodialysis: 10
Number of ESRD patients currently in post-transplant care: 10

Total Number of Patients In Registry: 44
Number of active Patients in Registry: 13

Local IPPN Investigators:
Dr. Loai Eid
Dr. Hazem Subhi Awad

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INTRODUCTION & BACKGROUND

• The nutritional status is a concern when caring for children undergoing chronic peritoneal dialysis (CPD)

• Children approaching end-stage kidney disease (ESKD) are considered at risk of uremic anorexia and underweight they are also exposed to the global obesity epidemic

• Recent concerns have emerged on the potential for adverse effects of excessive caloric intake in patients who receive supplemental feeding
INTRODUCTION & BACKGROUND

- The majority of published studies assessing the nutritional status of dialyzed children were performed at highly specialized units in North America and Western Europe.

- On a global scale the risk of nutritional abnormalities in individual regions and countries is likely to be affected by a range of medical and non-medical factors including:
  - The patient case-mix regarding age
  - Underlying disease and co-morbidities
  - National economic strength and healthcare expenditure
  - Availability of special formula ic diets and enteral feeding equipment
  - Differences in local, national or regional nutritional recommendations
INTRODUCTION & BACKGROUND

- The IPPN has been collecting comprehensive clinical and laboratory data in a standardized manner from children undergoing CPD worldwide since 2007.

- These data include detailed **anthropometric measures**, **feeding prescriptions** and **outcome measures**, it provides an opportunity to address the global demographics of nutritional abnormalities in children receiving CPD.
OBJECTIVES

• To examine and follow *prospectively* the nutritional status of 1,001 children commencing CPD around the globe

• To analyze factors associated with the nutritional status at the start and during the course of dialysis

• To analyze the impact of nutritional abnormalities on patient survival
METHODS - DATA COLLECTION

• The IPPN Registry currently collects information from children undergoing CPD at 95 pediatadic dialysis centers in 37 countries around the globe

• Patient status is updated every 6 months via an Internet-based web platform (www.pedpd.org)

• Data is automatically checked for completeness. Data protection is ensured by pseudonymized data input

• Approval for the registry project was obtained from The Children's Mercy Hospital Paediatric IBR, Kansas City, USA and local IBRs or ethical committees

• Informed consent was obtained from the patients and/or their legal guardians
CALCULATION OF BMI SDS AND EGFR

• BMI, i.e. weight/height$^2$ (kg/m$^2$), was normalized to SDS according to height age, utilizing the WHO (2006) and CDC (2000) standards for children aged younger and older than 5 years, respectively.

• Normalization to height age, i.e. the chronological age of a child with the same height growing at the 50$^{th}$ height percentile, was made to adjust for the high prevalence of growth failure in the cohort.

• BMI SDS values were used to categorize patients into three BMI groups:
  - Underweight (<2.5$^{th}$ percentile, i.e. <-2 SDS)
  - Normal (2.5$^{th}$ to 85$^{th}$ percentile, i.e. -2 to 1.036 SDS)
  - Overweight (>85$^{th}$ - 95$^{th}$ percentile, i.e. >1.036 to 1.645 SDS) & Obesity (>95$^{th}$ percentile, i.e. >1.645 SDS)

• The Schwartz bedside formula was used to estimate GFR at initiation of CPD; (0.413xHt / Serum Creatinine)
**STATISTICS**

- **ANOVA or Kruskal-Wallis tests** were conducted to compare differences between BMI groups. Differences in proportions were assessed using Chi² tests.

- **Linear mixed modelling** was used to identify factors affecting BMI SDS at baseline and during follow-up.

- The initial cross sectional model included: **age, sex, eGFR, gross national income (GNI), renal diagnosis, ethnicity, urine output, nutritional support** (oral caloric supplements, nasogastric tube (NGT) and gastrostomy feeding), and **growth hormone** use as independent variables.
The longitudinal analysis, the change in BMI SDS between two observations, projected to 12 months, was used as the dependent variable.

Kaplan–Meier analysis with log-rank testing was used to assess differences in patient survival. Cox proportional hazard modelling with time dependent covariates and interaction term was applied to identify risk factors of death on dialysis.

Data were analyzed using SAS, version 9.3 (SAS Institute, Inc., Cary, NC), and R, version 3.1.1.
RESULTS - STUDY POPULATION

• **Inclusion criteria**: All children and adolescents enrolled in the IPPN registry with initiation of CPD between March 2007 and December 2014 were analyzed for this study

• **Exclusion criteria**: Five patients with syndromic and metabolic disorders associated with intrinsic abnormalities of growth and body composition

• **The final dataset comprised a total of 1,001 incident patients** from 85 nephrology centres in 35 countries
RESULTS - STUDY POPULATION

- Children originated from Western Europe (n = 300), Central Europe (n = 120), Turkey (n = 105), the Middle East (n = 15), China and Hong Kong (n = 77), Korea (n = 24), India and South East Asia (n = 30), New Zealand (n = 18), USA (n = 97), Canada (n = 13) and Latin America (n = 202)

- Of the 1,001 patients, 702 (70%) patients had at least two BMI records available. Altogether, the data set contained 2,931 follow-up entries

- Median follow-up time was 14.5 (IQR 17.8) months
The overall prevalence at the start of CPD was:
Underweight 8.9%,
Normal weight 71.4%,
Overweight/obesity 19.7%
Underweight was most prevalent in:
- South and Southeast Asia (20%)
- Central Europe (16.7%)
- Turkey (15.2%)

Overweight and obesity were most common in:
- Middle East (40%)
- US (33%)
NUTRITIONAL STATUS AT DIALYSIS INITIATION

• The prevalence of underweight was highest in the first year of life (14.2%), decreasing to 6.5%, 9.4% and 7.7% in children aged 1–<6, 6–12 and older than 12 years, respectively

• The prevalence of obesity was higher in the younger children than in adolescents

• BMI SDS at dialysis initiation was positively predicted by eGFR and the use of gastrostomy feeding and negatively predicted by the presence of comorbidities, other factors were not predictive
The prevalence of underweight was correlated with the eGFR at initiation of PD, increasing from 5.3% at eGFR 9–12 ml/min/1.73 m² to 11% at eGFR < 6 ml/min/1.73 m² (p = 0.03)
- Enteral (NGT or gastrostomy) feeding was used at baseline in 57.4%, 32.9%, 5.6%, and 2.3% of children <1, 1–<6, 6–12 and >12 years, respectively (p < 0.001)

- Gastrostomy usage was confined to North America, Western Europe, Korea and New Zealand
Out of 74 underweight children at the start of CPD, 51.4% were non-underweight at last observation.

Among 125 overweight/obese children at CPD initiation, 36.0% achieved a normal BMI at follow-up.
CHANGES IN NUTRITIONAL STATUS WITH TIME ON CPD

- Gastrostomy feeding was associated with an increase in BMI SDS during follow-up.

- Greater fluid overload was predictive of a negative change in BMI SDS during follow-up.

<table>
<thead>
<tr>
<th></th>
<th>Parameter Estimate (SE)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-0.056</td>
<td>0.89</td>
</tr>
<tr>
<td>Duration of PD (years)</td>
<td>-0.060</td>
<td>0.09</td>
</tr>
<tr>
<td>Diagnosis (reference: CAKUT)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glomerulopathy</td>
<td>-0.229</td>
<td>0.01</td>
</tr>
<tr>
<td>Other</td>
<td>-0.364</td>
<td>0.001</td>
</tr>
<tr>
<td>BMI SDS</td>
<td>-0.456</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Height SDS</td>
<td>0.113</td>
<td>(0.025)&lt;0.001</td>
</tr>
<tr>
<td>% deviation from estimated dry weight</td>
<td>-0.040 (0.014)</td>
<td>0.01</td>
</tr>
<tr>
<td>Serum albumin (g/L)</td>
<td>0.015</td>
<td>(0.006)0.02</td>
</tr>
<tr>
<td>Nutritional supplementation (reference: none)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral</td>
<td>-0.195</td>
<td>(0.090)0.03</td>
</tr>
<tr>
<td>NGT</td>
<td>0.122</td>
<td>(0.133)0.36</td>
</tr>
<tr>
<td>Gastrostomy</td>
<td>0.633</td>
<td>(0.132)&lt;0.001</td>
</tr>
</tbody>
</table>

Table 2. Factors predicting prospective annualized change in BMI SDS. Positive change means BMI SDS increase (702 patients, 1930 differences in BMI SDS).
NUTRITION AND MORTALITY

- 54 children died during the observation period. The most common causes of death were:
  - Non-PD related infections (39%)
  - Congestive heart failure (17%)
  - PD-related infections (7%) &
  - Malignancies (7%)
NUTRITION AND MORTALITY

- Cox proportional hazard analysis identified the presence of comorbidities and younger age as risk factors for death on dialysis.

Risk factors for death in CPD:

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Estimate</th>
<th>(SE)</th>
<th>Hazard Ratio</th>
<th>95% Confidence Interval</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comorbidity</td>
<td>0.836</td>
<td>(0.279)</td>
<td>2.307</td>
<td>[1.336, 3.987]</td>
<td>0.001</td>
</tr>
<tr>
<td>Age</td>
<td>-0.102</td>
<td>(0.028)</td>
<td>0.903</td>
<td>[0.856, 0.954]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI SDS</td>
<td>0.136</td>
<td>(0.123)</td>
<td>1.145</td>
<td>[0.900, 1.457]</td>
<td>0.27</td>
</tr>
<tr>
<td>BMI SDS * Age</td>
<td>-0.028</td>
<td>(0.015)</td>
<td>0.973</td>
<td>[0.945, 1.002]</td>
<td>0.06</td>
</tr>
</tbody>
</table>
NUTRITION AND MORTALITY

- In infancy, mortality risk was amplified by obesity, whereas in older children mortality was markedly increased in association with underweight.
CONCLUSIONS

• This study highlights a changing trend of the nutritional status in pediatric ESRD

• Both underweight and obesity are observed at increased frequency in pediatric ESRD

• Late dialysis start is associated with underweight, while enteral feeding can lead to obesity

• The most important single factor associated with higher BMI SDS both at PD start and during follow-up was the presence of a gastrostomy

• Nutritional abnormalities tend to attenuate with time on dialysis
THANK YOU

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