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**Abstract B:** Role of Fiberoptic Bronchoscopy and Bronchoalveolar Lavage in Immunocompromised Children  
**Abstract C:** Role of Fiberoptic Bronchoscopy and Bronchoalveolar Lavage in Immunocompromised Children - Clinical profile of children with cystic fibrosis surviving through adolescence | Bhawna Agarwal, Kanaram Jat, Rakesh Lodha, SK Kabra |
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Prevalence and predictors of malnutrition in children with cystic fibrosis

Authors

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Abstract

Introduction: Nutritional status in cystic fibrosis (CF) patients is important prognostic marker with good correlation with pulmonary functions. Children in developing countries are at increased risk of malnutrition due lack of specialists and high cost of therapy.

Aims & Objectives: The primary objective of the study was to estimate prevalence of malnutrition in children with cystic fibrosis.
The secondary objectives were: 1) To determine predictors of malnutrition at the time of enrolment in the clinic and after completing 2 years of follow up in chest clinic; and 2) To study association between nutritional status and pulmonary exacerbation rate.

**Materials and methods:** Retrospective chart review of CF patients enrolled in pediatric chest clinic form tertiary care centre in North India with at least 3 years follow-up were included. Weight and height were noted at enrolment, and 1 and 2 years of follow-up. “WHO Anthroplus” was used to calculate the Z-scores for anthropometry [weight for age Z score (WAZ), height/length for age Z score (HAZ) and body index for age Z score (BAZ)]. Clinical details (gastrointestinal and pulmonary symptoms), medications, and pulmonary exacerbations during second year were recorded.

**Results:** Sixty-one children (64% boys) were enrolled. Prevalence of malnutrition (WAZ < -2) at baseline, and at 1- and 2-year follow up was 65.5%, 54.1% and 57.3%, respectively. WAZ, HAZ and BAZ over first year showed significant improvement (p-value of < 0.001, 0.021, 0.005, respectively). But during second year, while improvement was not seen in WAZ (p-value of 0.889), HAZ showed improvement (p-value = 0.024) and BAZ showed decline (p-value= 0.022).

WAZ at enrolment was significantly associated with time to diagnosis form onset (coefficient=0.015, p=0.029). WAZ at 2 years follow-up was significantly associated with steatorrhea, increased frequency of stools and pulmonary exacerbation during second year (p = 0.031, 0.004, 0.027). Linear regression showed significant association between WAZ at 2 years with steatorrhea and pulmonary exacerbations, co-efficient -0.795 (-1.527, -0.062) and -0.261(-0.493, -0.028) respectively. Overall pulmonary exacerbations during second and third year had significant correlation with WAZ at the beginning of years (coefficient= -0.219,
p=0.015). Pulmonary exacerbations during second year was significantly associated with Shwachman-Kulczycki score (p=0.020).

**Conclusion:** Prevalence of malnutrition is very high in children with CF in North India. Uncontrolled fat malabsorption and recurrent respiratory infections during follow up have significant negative impact on nutritional status. Efforts are needed for improved nutritional support, improve affordability of pancreatic enzyme replacement therapy to control steatorrhea and avoid pulmonary exacerbations for better nutritional outcome and overall health of children with CF.
**SR-81B**

**Lentil Aspiration Causing Hypersensitivity Pneumonitis: Describing A Novel Antigen, Novel Entity**

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**Introduction:** Childhood interstitial lung disease is an uncommon entity, with hypersensitivity pneumonitis (HP) being an important presentation. Variety of inhaled antigens have been implicated in pathogenesis of HP in children. Also occult aspiration has been described to cause pulmonary fibrosis but aspiration is not described as a common mechanism for HP. We observed that children who had aspiration due to lentil based weaning food had persistent respiratory symptoms and radiological phenotype similar to HP.

**Objectives:** To describe clinical course, treatment and outcome of children with lentil aspiration HP.
Materials & methods: We conducted a retrospective review of records from Pediatric Chest Clinic at tertiary care hospital in North India, of children with persistent respiratory symptoms following aspiration due to force-feeding of lentil containing feeds. Clinical signs and symptoms, laboratory investigations, treatment details, and outcome were noted in predesigned pro-forma. All children were treated with systemic steroids with clinical and radiological monitoring. Some children were tested for IgG specific for lentil antigens.

Results: Sixteen children (13 boys) who experienced prolonged respiratory symptoms following forced feeding of lentil containing feeds were included. Median (IQR) age of onset of symptoms and diagnosis was 9 (6, 13) months and 11 (9.5, 16.5) months, respectively. Chronic cough was present in all children with median duration of 2 months (range 1-9 months); the nature of cough was dry in 14 (87.5%) children. Breathlessness and fever were next most common symptoms with frequency of 93.7% and 87.5%, respectively. Other symptoms were vomiting and wheezing (37.5% and 25%, respectively). Empirical anti-tubercular drugs had been given in 9 out of 13 (69.2%) children with available data. Fine crepitations were heard in 4 (25%) children, none
Predictors of Mortality in Children admitted to the Paediatric Intensive Care Unit with Acute Gastroenteritis with Severe Dehydration

Authors: Arvind Kumar, MD; Man Singh, MD; Jhuma Sankar, MD; U Vijay Kumar; Rakesh Lodha, MD; SK Kabra, MD

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Source of support: Nil

Running title: Predictors of mortality in children with diarrhoea

Conflict of Interest: On behalf of all authors, the corresponding author states that there is no conflict of interest.

Word count: Abstract: 224

Key words: Diarrhoea; dehydration; mortality; acute gastroenteritis; AGE; hypoalbuminemia; ORS
Abstract

**Objective:** Our objective was to identify risk factors for mortality at admission in children with acute gastroenteritis (AGE) with severe dehydration and shock.

**Methods:** This was a retrospective chart review of all cases of AGE with severe dehydration and shock admitted to the Paediatric Intensive Care Unit (PICU) from 2012-2017. Children who died during hospital stay were compared with those who survived. Information including demographic details, nutritional status, clinical features, laboratory parameters and clinical course were recorded. Data were analysed using Stata11.

**Results:** A total of 62/ 1469 (4.2%) children were admitted to the PICU with AGE with severe dehydration and shock during this period. Majority (56%) were males and were from urban slums (71%). Forty three % had Severe Acute Malnutrition (SAM). Twenty-four children (39%) died. The following variables were found to be significantly associated with death on univariate analysis: clinical pallor (0.01), thrombocytopenia (0.018), elevated leucocyte count (0.02), hypoalbuminemia (p=0.02) and nutritional status (SAM) (p=0.04). On multivariate analysis, only hypoalbuminemia [RR (95% CI): 4.1 (1.24, 16.2); p=0.03] and SAM status (12.1 (1.14, 18); p=0.04) remained statistically significant.

**Conclusion:** The case fatality rate of AGE with severe dehydration and shock continues to be high despite increased awareness and better formulations of Oral Rehydration Solution available in the current era. Severe Acute Malnutrition status and hypoalbuminemia are associated with increased risk of death in these patients.

**Keywords:** Acute gastroenteritis; AGE; shock; hypoalbuminemia; ORS; oral rehydration solution
Role of Fiberoptic Bronchoscopy and Bronchoalveolar Lavage in Immunocompromised Children

Arvind Kumar, Kana Ram Jat, Jhuma Sankar, Rakesh Lodha, SK Kabra
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Word counts: 338

Funding: None

Conflict of interest: None

Role of Fiberoptic Bronchoscopy and Bronchoalveolar Lavage in Immunocompromised Children

Abstract

Introduction: It is difficult to diagnose and plan further therapeutic procedures for pulmonary disease in immunocompromised children because of diversity of possibilities of infectious etiologies. Many non-infectious conditions also present similar to infectious etiologies. In these children, making a definite diagnosis based on clinical findings, chest x ray and computerized tomography (CT), is
challenging. In such cases, bronchoscopy and bronchoalveolar lavage are important in improving the diagnostic yield and detection of pathogen.

**Aim and objective:** To evaluate the utility of bronchoscopy and specialized investigation on bronchoalveolar lavage sample (PCR for cytomegalovirus (CMV)/ Pneumocystis jiroveci (PJP), MGIT, Genexpert, Galactomannan) were done in addition to routine bacteriology and cytology investigations in making diagnosis and management of lung disease in immunocompromised children.

**Material and methods:** A retrospective review of 136 bronchoscopy and BAL procedures performed during last 5 months (May to September 2018) in Pediatrics department, AIIMS, Delhi, was carried out. The demographic characteristics of cases, indications for procedures, type of procedure performed (BAL sampling), complication during procedure, results of sampling and final diagnosis were recorded. The overall safety and rate of diagnostic yield of specialized BAL investigations in immunocompromised children were determined.

**Results:** Out of 136 bronchoscopy and BAL procedures during study period, 18 procedures were performed in immunocompromised children and were included in the study. Use of specialized BAL investigations led to a diagnosis in ten (55%) children. Out of these 10 diagnosis, invasive aspergillosis was identified in six (6/18, 33%) children, and bacterial and viral (CMV) pathogens in four (4/18, 22%) children each. Two BAL samples (11%) had positive result of PCR for Pneumocystis Jirovecii Pneumonia (PJP). Following positive BAL sample results, therapy was modified in seven (39%) children with positive BAL results and therapy was adjusted in eight (44%) children due to negative BAL results. The procedures were well tolerated.

**Conclusions:** Bronchoscopy and BAL is a useful investigation in improving diagnostic yield in immunocompromised children with pulmonary conditions.

**Key words:** Pulmonary disease, immunocompromised children, bronchoscopy, bronchoalveolar lavage.
Clinical profile of children with cystic fibrosis surviving through adolescence and beyond

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Word counts (Abstract) 255 ,

Short title: Clinical profile of adolescents with cystic fibrosis

Contribution of authors: AK: data analysis, written manuscript, BA: data collection, analysis, manuscript writing, KRJ: manuscript writing, RL: Data analysis, review of manuscript, SKK manuscript writing, will act as guarantor for manuscript

Competing interest: None

Funding: None

Abstract

Introduction: Cystic fibrosis a multisystem autosomal recessive inherited disease considered as nonexistent in India till few decades ago. More recently it is emerging disease in India. Average survival of children with CF has improved. There is no study to documents morbidities in adolescents with CF from India or similar resource limited setting.

Aim and objective: To document clinical profile, complications of children with CF surviving beyond 15 years of age.

Material and methods: A retrospective chart review of children with cystic fibrosis more than 15 years of age attending Cystic fibrosis services in pediatric Chest Clinic of All India Institute of Medical Sciences was carried out. Details of demography, clinical profile, course of illness, laboratory parameters were extracted in predesigned Performa and analyzed.

Results: A total of 42 children survived beyond 15 years of age. 30 children were surviving at time of study. Ratio of male to female of this study
population was 1.33 and 21% children had family history of CF. Delta 508 mutation was positive in 21% children. All patients were on pancreatic enzyme supplement, fat soluble vitamin supplement and hypertonic saline inhalation along with chest physiotherapy. A total of 33% children were getting inhaled antibiotics also. 85% children showed airway colonization by pseudomonas species and 26% children developed cystic fibrosis related diabetes (CFRD). 21% children developed allergic bronchopulmonary aspergilosis (ABPA). The distal intestinal obstruction syndrome (DIOS) was diagnosed in 11% children. Only patient had delayed puberty.

Conclusion: With increasing age children with CF developed colonization with pseudomonas, CFRD, DIOS and ABPA. This study will help physician to looking after children with CF.

Key words: Cystic fibrosis, CFTR mutation, sweat chloride test, delayed diagnosis, pancreatic enzyme replacement, India
**SR-83**

**Oral tolvaptan with intravenous (IV) furosemide for refractory edema in patients with nephrotic syndrome: A prospective interventional study**

Meena Jitendra, Sinha Aditi, Hari Pankaj, Bagga Arvind  
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**Introduction:** Severe edema in patients with nephrotic syndrome is often refractory to conventional diuretics and predisposes to complications. Tolvaptan, an aquaretic has been used satisfactorily for managing edema in patients with heart failure and cirrhosis.

**Aim and objective:** To assess the safety and efficacy of the combination of oral tolvaptan and IV furosemide in patients with refractory edema due to nephrotic syndrome.

**Methods:** Patients, 3-18 years old, with nephrotic syndrome and severe edema requiring inpatient admission were assessed for eligibility. After excluding hypovolemia, patients received IV furosemide (3-4 mg/kg/day) for 48 hr. Those refractory to IV furosemide (weight loss <5%) received oral tolvaptan (0.5-1 mg/kg once daily; maximum 30 mg) and IV furosemide for next 48 hr. Parameters were compared between 48 hr of IV furosemide alone and with tolvaptan.

**Results:** During September 2017 to November 2018, 20 patients (13 boys), mean age 8.6±3.7 years, were enrolled. Compared to therapy with IV furosemide, combination with oral tolvaptan was associated with significant reduction in body weight (mean difference -2.1 kg; 95% CI: 1.3-2.9; P<0.0001) and increase in urine output (715 ml/day; 95% CI: 447-983, P<0.0001) (Table1). The estimated glomerular filtration rate did not change (P=0.35) but serum sodium increased (mean difference 4.6±4.0 mEq/L; P=0.001) with combination; one patient showed hypernatremia. There was no significant change in urinary sodium and potassium excretion (both P>0.05). Therapy was discontinued for hypovolemia in one, and excessive weight loss in two patients.

**Conclusion:** The combination of oral tolvaptan and IV furosemide is effective in enabling diuresis and reducing edema in patients with refractory nephrotic edema but requires monitoring of electrolytes and volume status.
<table>
<thead>
<tr>
<th>Parameters</th>
<th>After IV furosemide for 48 hr</th>
<th>After oral tolvaptan and furosemide for 48 hr</th>
<th>P-value*</th>
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<tr>
<td>Weight loss (%)</td>
<td>3.6±1.3</td>
<td>7.2±3.6</td>
<td>&lt;0.001</td>
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<td>Urine volume (mL/day)</td>
<td>1007±395</td>
<td>1755±630</td>
<td>&lt;0.001</td>
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<tr>
<td>Hematocrit (%)</td>
<td>37.2±7.2</td>
<td>37.8±4.8</td>
<td>0.83</td>
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<tr>
<td><strong>Blood</strong></td>
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<tr>
<td>Sodium (mEq/L)</td>
<td>136±3.4</td>
<td>140±3.6</td>
<td>&lt;0.001</td>
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<tr>
<td>Urea (mg/dL)</td>
<td>49±24</td>
<td>40±22</td>
<td>0.75</td>
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<tr>
<td>Albumin (g/dL)</td>
<td>1.2±0.2</td>
<td>1.5±0.3</td>
<td>0.002</td>
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<tr>
<td>eGFR (mL/min/1.73 m²)</td>
<td>133 (77-165)</td>
<td>160 (84-201)</td>
<td>0.35</td>
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<tr>
<td><strong>Urine</strong></td>
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<tr>
<td>Sodium (mEq/L)</td>
<td>113 (53-198)</td>
<td>90 (51-164)</td>
<td>0.87</td>
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<tr>
<td>Potassium (mEq/L)</td>
<td>24 (17-37.5)</td>
<td>28 (17-33)</td>
<td>0.11</td>
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<tr>
<td>Osmolal clearance (mL/day)</td>
<td>1180 (792-1361)</td>
<td>1705 (1140-2142)</td>
<td>0.91</td>
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<td>Free water clearance (mL/day)</td>
<td>4.6 (-217, 95)</td>
<td>-40 (-220,344)</td>
<td>0.32</td>
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</table>

Value represent median (interquartile range) or mean (±sd)

* Wilcoxon sign rank test or paired t test

eGFR estimated glomerular filtration rate
Title-Comparison of Efficacy of Daily and Intermittent Low Glycemic Index Therapy Diet among Children with Drug Resistant Epilepsy aged 1-15 years: A Randomized Controlled Non-inferiority Trial

Authors-

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Abstract body

Introduction-Efficacy of Low Glycemic Index Therapy (LGIT) is currently well established in children with Drug Resistant Epilepsy (DRE). However, predominant reason for its discontinuation is dietary restrictions imposed therein. Hence, allowing liberalized diet for 1-2 days every week is likely to improve compliance and reduce discontinuation rate with LGIT.

Aims and objectives-Primary objective of the current RCT (NCT03464487) was to compare the efficacy of daily and intermittent LGIT in children aged 1-15 years with drug resistant
epilepsy, following 24 weeks of dietary therapy. Compliance, difficulty faced by caregivers, adverse effects, impact on behavior and social quotient in both arms were also compared. Blood HbA1c and Beta hydroxy butyrate (BHB) levels were determined in both groups at 0, 12 and 24 weeks and their values were correlated with seizure frequency reduction.

**Methods** - Children with DRE (at least 2 antiepileptic drugs failed) were enrolled between February-December 2018, after excluding inborn error of metabolism, chronic systemic illness and candidates for epilepsy surgery. In daily LGIT arm, children received only low glycemic index (GI) foods daily, with about 10% of daily calories from carbohydrate. Children in intermittent LGIT arm received a liberalized diet for two days every week (Saturday and Sunday), which allowed both medium and low GI foods and about 20% calories from carbohydrate. Behavior and social quotient were evaluated at baseline and 24 weeks by using Child Behavior Checklist and Vineland social Maturity Scale respectively.

Compliance was assessed on follow up visits at 4, 12 and 24 weeks, by three days dietary record documentation by caregiver. Children with >80% compliance are considered to have satisfactory compliance. A self administered questionnaire with 10 questions, each having 5 graded options, filled by caregiver at the end of dietary therapy was utilized to evaluate the difficulty in complying with dietary restrictions in each arm.

**Results** - Out of the 141 children screened, 9 were excluded and 66 children were enrolled in each arm, by age stratified, variable block randomization. 60 and 62 children in daily and intermittent LGIT arm completed 24 weeks of dietary therapy respectively. Mean weekly seizure frequency reduction in daily and intermittent LGIT arms were 50.95±22.34% & 47.16±23.41% (intention to treat analysis) and 53.88±20.54% & 49.20±21.87% (per protocol analysis) respectively. Thus, intermittent LGIT was found to be non-inferior to daily LGIT at a non-inferiority margin of -15%.

No significant difference was found between improvement in behavior and social quotient, as well as frequency of various adverse effects in both arms (p=0.36, 0.31 and 0.12 respectively). Difficulty in complying with dietary restrictions was more with daily LGIT (32.4±4.6), as compared to intermittent LGIT (26.9±3.7, p= 0.001). Larger proportion of children on intermittent LGIT had satisfactory compliance (83% vs 79%), although the difference was not statistically significant (p=0.51). Percentage HbA1c reduction at 12 and 24 weeks (r=0.78 and 0.52) and BHB level at 12 and 24 weeks (r=0.83 and 0.73) had good positive correlation with mean weekly seizure frequency reduction.

**Conclusion** - Intermittent LGIT is non-inferior to daily LGIT in terms of seizure frequency reduction after 24 weeks of dietary therapy.
PROOF-OF-CONCEPT STUDY TO ASSESS THE EFFICACY OF 3 DAYS INTRAVENOUS CEFTRIAXONE FOLLOWED BY SWITCH TO ORAL CEFIXIME FOR UNCOMPLICATED SPONTANEOUS BACTERIAL PERITONITIS IN CHILDREN WITH NEPHROTIC SYNDROME

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Introduction: Spontaneous bacterial peritonitis (SBP) is a common complication of nephrotic syndrome. Empirical therapy consists of intravenous (IV) ceftriaxone for 5-7 days. We conducted a proof-of-concept study to evaluate the efficacy of short course IV ceftriaxone in SBP.

Objectives: To assess the efficacy of 3-day IV ceftriaxone followed by oral cefixime in uncomplicated SBP in nephrotic children as assessed by the proportion of patients having resolution of clinical features of SBP till day 24 of follow-up and to determine the proportion of patients with treatment failure.

Methods: Children aged 3-18 years, admitted with nephrotic syndrome and uncomplicated SBP were treated with 3 days of IV ceftriaxone and on improvement were switched to oral cefixime for 7 days and followed up for another 2 weeks. Peritoneal diagnostic tap for cytology, Gram stain, culture and leukocyte esterase test and blood investigations were performed. Data were entered in MS excel. Statistical analysis was done using Stata software (version 13).

Results: Between October 2017 to December 2018, 26 children (median age 6.6 years) were initially included for IV ceftriaxone, 5 were excluded from oral switch at 72 hours (3 co-infection, 2 persistent symptoms). The baseline clinical characteristics and laboratory
investigations were not significantly different between patients who were treated with ceftizime vs who were not switched. The median ascitic cell count was 7865/mm$^3$ (9558 in ascitic culture positive vs 2350 in negative; p=0.67). Leucocyte esterase and Gram stain of ascitic fluid were positive in 52.4% and 28.6%. All the 21 patients treated with ceftizime had clinical resolution of SBP. None had recurrence of SBP till last follow-up (day 24). No severe adverse events were noted with ceftizime.

**Table: Comparison of investigations between oral ceftizime switch vs no switch**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Oral switch (n=21)</th>
<th>No oral switch (n=5)</th>
<th>P value</th>
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<tbody>
<tr>
<td>Age (months)</td>
<td>81(60,114)</td>
<td>123(66,144)</td>
<td>0.42</td>
</tr>
<tr>
<td>Ascitic cell count (per mm$^3$)</td>
<td>7865(165,16000)</td>
<td>300(300,420)</td>
<td>0.24</td>
</tr>
<tr>
<td>TLC (per mm$^3$)</td>
<td>17700(11600,21100)</td>
<td>18400(11200,18700)</td>
<td>0.74</td>
</tr>
<tr>
<td>CRP(mg/l)</td>
<td>105.5(18,146)</td>
<td>49.3(12,133)</td>
<td>0.83</td>
</tr>
<tr>
<td>Procalcitonin(ng/ml)</td>
<td>5.95(0.29,17.36)</td>
<td>1.07(0.14,3.14)</td>
<td>0.39</td>
</tr>
<tr>
<td>Positive ascitic culture</td>
<td>6/21</td>
<td>0/5</td>
<td></td>
</tr>
</tbody>
</table>

*Values are median(IQR)*

Ascitic fluid culture was positive in 28.6% (2 Streptococcus pneumonia, 1 each for Acinetobacter baumanii, Enterococcus faecalis, Escherichia coli and Staphylococcus hominis) and 67% of them were sensitive to ceftizime. TLC, CRP and procalcitonin were not different among ascitic culture positive and negative group. There was moderate correlation between ascitic cell count and improvement in procalcitonin ($r = 0.68$); but poor correlation with blood TLC, CRP, procalcitonin, albumin and cholesterol.

**Discussion and conclusion:** Majority (80.8%) of the uncomplicated SBP could be switched to oral ceftizime after 3 days of IV ceftizime. Therapy with ceftizime had lead to clinical remission of SBP which might result in shorter hospital stay and reduced IV antibiotic use, thus lowering the cost of therapy.
Prevalence of sleep disordered breathing among Indian children with Down syndrome - A cross sectional study


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Introduction: Down syndrome (DS) is the most common chromosomal anomaly worldwide and these patients are at high risk of developing sleep disordered breathing (SDB) as compared to general population. Various studies have stated the prevalence of sleep disordered breathing in DS children ranging from 59% to 80% worldwide. Even with this high prevalence of SDB, there are no published studies regarding the prevalence of SDB among Indian children with DS. Given the multitudes of established co morbidities associated with DS, SDB is often a neglected entity, management of which may have significant impact in the cognitive, developmental and behavioural domains of these children. Though Polysomnography is the gold standard used for diagnosis of SDB the lack of widespread availability is a hindrance especially in resource poor setting like ours. So using a screening tool like a sleep questionnaire in the diagnosis of these disorders have to be assessed.

Objective: a) To study the prevalence of various sleep disorders among children with Down syndrome by overnight polysomnography b) To assess the utility of Pediatric sleep questionnaire (PSQ) as a screening tool in the diagnosis of SDB in children with DS.

Materials and methods: In a cross sectional study conducted at a tertiary centre in north India 53 children with DS were assessed for SDB by overnight PSG. Children who were clinically or karyotypically diagnosed as DS registered in the Genetics and birth defects clinic, Department of Pediatrics, AIIMS in the age group 3-12 years were included. Studies were scored in a three tier system by sleep technologists, by Sleep Scientist Dr. AG and by Dr GS according to AASM 2007 guidelines. PSQ was answered by the parents of all subjects with assistance from the investigator and the total score calculated at the end.

Observation and results: Out of 53 subjects (34 boys and 19 girls), 51 (96%) were found to have OSA. Mean Apnea Hypopnea Index (AHI) was 8.96± 1.8. Severity distribution was as following; mild OSA-26.4%, moderate OSA-35.8% and severe OSA-34%. Median sleep latency was found to be 30.2 minutes (22.4 to 38) and median sleep efficiency was 87.9% (82.1%-93.7%). Median arousal index was 14.6 (10.4-18.8). The sensitivity of PSQ in diagnosing OSA was 33.3% (20.76% - 47.92%). The specificity for PSQ was found to be 100% (15.81% - 100%). Positive predictive value also was 100% (80.49%-100%) and negative predictive value was 5.6% (0.68%-18.66%). Negative likelihood ratio was 0.67(0.55-0.81).

Conclusion: This study reveals a very high prevalence of OSA in Indian children with DS. This study has shown that PSQ cannot be used as a screening tool for SDB in children with DS and overnight PSG should be the modality of choice for proper assessment and stratification of sleep disorders in these children. This signifies the need for active search for OSA in children with DS and early management given its significant association between
behavioural problems and development. This becomes more important since most of the hospitals across India do not have screening for SDB as a part of the management protocol for children with DS.
Clinical outcomes and Coexisting variations in complement regulatory genes in anti-factor H antibody associated atypical hemolytic uremic syndrome

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Background: Atypical hemolytic uremic syndrome (aHUS), an important cause of acute kidney injury, is characterized by dysregulation of the alternative complement pathway. Autoantibodies to factor H (FH), a chief regulator of this pathway, account for a distinct subgroup. Patients with anti-FH associated aHUS, comprising one-half of children with aHUS, are managed by intensive PEX and immunosuppression. While deficiency of FH related protein-1 (CFHRI) is strongly associated, prevalence of additional variations is unclear and has implications for therapy. Long-term renal and cardiovascular outcomes are unclear.

Method: Of 435 children with anti-FH antibodies in the nationwide database; 93 (21.4%) were screened by targeted sequencing. A panel of 27 genes included entire regions of CFH, CFI, CFB, C3, CD46, THBD & DGKE. Functional renal reserve, ambulatory hypertension, left ventricular hypertrophy (LVH) and proteinuria were evaluated in a subset with eGFR > 60 mL/min/1.73 m\textsuperscript{2} after 2-years follow-up. Adverse outcome was eGFR<30 mL/min/1.73 m\textsuperscript{2} or death.

Results: Variants, chiefly of unknown significance (VUS), were found in 7.5\% (95\% CI 3.7-14.7; Table). In a systematic literature search of 14 studies (296 patients, including current study), the pooled prevalence of coexisting variations in a random-effect model was 5 (95\% CI, 1-12)\%; $I^2=67.6\%$ in patients with anti-FH antibody associated disease. Multiplex ligation-dependent probe amplification revealed homozygous deletion of CFHRI and 3 in 86\%; one had duplication of both and 4 had homozygous CFHRI deletion. After a follow-up of 34.5 (IQR 17.1-63.9) months, 33\% showed a disease relapse. A polymorphism in MASP1 (c.*822C>T) protected against relapses (allele frequency in relapsers vs. non-relapsers 0.015
vs. 0.11; \( P=0.02 \)). Coexisting variations independently increased relapse risk (HR 4.94; \( P=0.01 \)). Combined PEX & immunosuppression improved long-term outcomes, independent of genetic defects (HR=0.06; \( P=0.039 \)). At 4.4±2.5 yr, median renal reserve was 15.9%; severe ambulatory, masked and pre-hypertension were found in 38%, 30% and 18%, respectively. Proteinuria and LVH occurred in 58% and 28% patients, respectively.

**Conclusion:** Coexisting variations in complement regulatory genes predisposes to relapses in a small proportion of patients with severe anti-FH associated aHUS; PEX and immunosuppression improves outcomes. A significant proportion of impaired functional reserve, ambulatory hypertension, proteinuria and LVH highlight the need for vigilant long-term follow-up.

<table>
<thead>
<tr>
<th>Variant (all heterozygous)</th>
<th>Pathogenicity</th>
<th>Age, yr</th>
<th>Features</th>
<th>C3, mg/dl</th>
<th>Anti-FH, AU/ml</th>
<th>Relapse</th>
<th>eGFR &amp; outcome at follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CFI:</strong> c.148C&gt;G, p.P50A</td>
<td>Pathogenic^</td>
<td>4</td>
<td>Jaundice, GI prodrome</td>
<td>74</td>
<td>8800</td>
<td>One at 24 mo</td>
<td>82 at 14 yr, hypertension</td>
</tr>
<tr>
<td><strong>THBD:</strong> c.127G&gt;A, p.A43T</td>
<td>Likely pathogenic^</td>
<td>6</td>
<td>Nephrotic proteinuria</td>
<td>42</td>
<td>16133</td>
<td>One at 6-mo</td>
<td>ESRD by 9-mo</td>
</tr>
<tr>
<td><strong>DGKE:</strong> c.685G&gt;A, p.G229R</td>
<td>VUS, rare</td>
<td>9</td>
<td>Seizures, transient hemiparesis</td>
<td>89</td>
<td>4260</td>
<td>No</td>
<td>89 at 21-mo; hypertension, proteinuria</td>
</tr>
<tr>
<td><strong>CFI:</strong> c.193T&gt;C, p.Y65H</td>
<td>VUS; rare</td>
<td>9</td>
<td>Seizures, nephrotic proteinuria</td>
<td>40</td>
<td>7956</td>
<td>One at 6-mo</td>
<td>43 at 11-mo; hypertension;</td>
</tr>
<tr>
<td><strong>THBD:</strong> c.596C&gt;A, p.A199D</td>
<td>VUS; novel</td>
<td>4</td>
<td>Nephrotic proteinuria</td>
<td>40</td>
<td>26741</td>
<td>One at 9-mo</td>
<td>84 at 44-mo; hypertension, proteinuria, LVH</td>
</tr>
<tr>
<td><strong>C3:</strong> c.1402G&gt;A.p.G468R^</td>
<td>VUS; novel</td>
<td>7</td>
<td>Seizures, cardiogenic shock</td>
<td>43</td>
<td>3215</td>
<td>3 at 2.6 &amp; 24-mo</td>
<td>64 at 66-mo; hypertension</td>
</tr>
<tr>
<td><strong>CD46:</strong> c.608T&gt;C, p.I203T</td>
<td>Likely pathogenic^</td>
<td>11</td>
<td>Jaundice, anemia</td>
<td>85</td>
<td>1840</td>
<td>One at 12-mo</td>
<td>90 at 72-mo</td>
</tr>
</tbody>
</table>

*No CFHR1/3 homozygous deletion; ^in-vitro functional assay, #associated with low cell surface expression of protein*
Title: THE SPECTRUM OF GENETIC DIAGNOSIS IN EARLYONSET EPILEPTIC ENCEPHALOPATHIES


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Introduction: The diagnosis of Early onset epileptic encephalopathies (EIEE) poses a significant challenge to a neurologist. A significant number of EIEEs which are not associated with any neurometabolic or structural substrate are now being diagnosed on a genetic basis. In this study we have explored the spectrum of genetic etiologies in EIEE.

Methods: A retrospective review of case presenting to Pediatric Neurology Clinic at a tertiary care institute was done from January 2016 to May 2017. Data was collected on a pre-structured format.

Results: A total of 226 cases presenting with EIEE were identified during the study period. Of these 120 and 116 patients had seizure onset in the age groups of <6 months and 7-24 months respectively. 169 cases had an underlying structural etiology. Of the 57 cases without a structural substrate, 2 were diagnosed on metabolic studies (subsequently genetically confirmed). Only 46 of the 56 patients underwent genetic testing due to financial constraints. Genetic diagnosis could be reached in 24/27 (88%) cases presenting in < 6 months age group and 13/18 (72%) patients presenting between 7-24 months total (37/46; 80%). Channelopathies were the most common etiology in our cohort (SCN1A (n=7), SCN2A (n=3), KCNT1 (n=2) & GRIN2A (n=2). Although uncommon, severe microcephaly was invariably associated with encephalopathy and multiple seizure semiologies. No association was observed between the seizure semiology and genetic diagnosis.
Conclusion: Sodium channelopathies are the most common genetic mutation associated with IOEE in this cohort. A prospective study with adequate sample size is currently ongoing to further identify common genetic aetiologies and establish phenotype-genotype correlation.
Aim: To evaluate the effectiveness of Cisplatin monotherapy and compare it with PLADO in the treatment of standard risk Hepatoblastoma (SRHB)

Materials and Methods: Prospectively maintained data of patients of SRHB managed in the pediatric solid tumor clinic from June 2007 through December 2016 was analyzed. Efficacy of Cisplatin monotherapy (monotherapy) as the only chemotherapy (both as neoadjuvant and adjuvant) was compared to PLADO in terms of 5-year overall survival (OS) and recurrence rates and 5-year recurrence free survival (RFS).

Results: Of the 62 HB patients treated in this period, 32 (51.6%) were SRHB. Nineteen of these 32 (59.4%) were started on monotherapy but 6 were subsequently upgraded to PLADO due to poor response. Therefore, 13/32 (40.6%) got exclusive monotherapy (both neoadjuvant and adjuvant), while 19/32 (59.4%) received PLADO (including 6 upgraded from monotherapy). Overall of the 32 SRHB patients, 31 could be resected, while 1 died pre-operatively (discontinued treatment after 2 courses and then reappeared after 5 months with massive tumor and died the next day). Twenty-nine of 32 (90.6%) SRHB were alive (28CR; 1 progressive recurrent disease) and 3 (9.4%) had died (1 pre-op; 1 immediate post-op; 1 progressive recurrence). Among the 32 SRHB, there were 5 (15.6%) recurrences giving a 5-year OS 0.89 (0.71-0.96), RFS 0.79 (95CI 0.56-0.91). Of these 5 recurrences, 3 are in CR after salvage therapy (Irinotecan+surgery), 1 has died (after three courses of Irinotecan with unresectable local recurrence) and 1 was alive at last FU with progressive local recurrent disease. Among the 13 monotherapy alone, all were alive in complete remission (CR) with no
recurrences (5-year OS and RFS 1.0). Among the 19 who got PLADO, 16(84.2%) were alive (15 CR; 1PD) while 3(15.8%) had died. There were 5(26.3%) recurrences giving a 5-year OS 0.82(95CI 0.55-0.94), RFS 0.62(95CI 0.3-0.8). Among the 6 monotherapy patients who were upgraded to PLADO, only 4(66.7%) were alive(3CR; 1Progressive recurrence), while there were 2 (33.3%) deaths. There were 3(50%) recurrence giving an OS 0.62(95CI 0.14-0.89; HR 8.9, p = 0.08), RFS 0.28(95CI 0.01-0.7; HR 11.8, p = 0.008). Thirteen SRHB patients got PLADO from the very beginning. Among these thirteen, 12(92.3%) were alive (all CR), while there was only 1(7.7%) death (Pre-operative death). There were 2 (15.3%) recurrences, both of whom were alive in CR after recurrence management. This gave a 5-year OS of 0.92 (95CI 0.56-0.99) and RFS 0.75(95CI 0.25-0.9).

**Conclusion:** The outcome of SRHB patients was good with a 5-year OS and RFS being 0.89 and 0.79. All the SRHB patients treated with monotherapy alone could be resected and had 5-year OS of 100% with no recurrences. SRHB patients who were upgraded from monotherapy to PLADO, when compared to the ones who received PLADO from the beginning did much worse(OS 0.62 vs 0.92 and RFS 0.28 vs 0.75). Patients who were upgraded, because of poor response to monotherapy, ultimately had the poorest outcome. Even after upgrading to PLADO these patients had not done well with higher recurrences.
SR-90

TELOMERASE ACTIVITY IN WILMS’ TUMOR AND ITS PROGNOSTIC VALUE

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Introduction and purpose: Telomerase expression has been proposed as a tumor marker associated with poor outcome in a number of adult and pediatric malignancies.

Aim: This study was undertaken to examine the telomerase activity in wilms’ tumor.

Material and Methods: Telomerase activity was studied on the tumor tissue obtained from cases of Wilms’ tumors registered and treated at the hospital from February 2006 through February 2007. Telomerase activity was done using the PCR ELISA kit. Statistical analysis was carried out using STATA 9.0. Data were presented as number (%) and median (range) as appropriate. The difference in proportions were compared using chi-square / Fisher exact test. The differences in medians were compared using Wilcoxon Ranksum test. Overall survival was calculated using Kaplan-Meier method and it was reported as survival rate (95% CI). The p value <0.05 is considered statistically significant.

Results: Twenty-four specimens from 22 cases (2 were bilateral) were studied. Using 0.2 as cut-off for positive telomerase activity, 19 of 24 samples were positive (79.2%) and 5 of 24 (20.83%) were negative. Four of these 5 negative samples were from patients who had received pre-operative chemotherapy. The median telomerase activity in the tumor tissue was 0.649 (range of 0.031-2.382). Telomerase activity in adjacent normal kidney tissue was 0.265 (range 0.012-0.714). This difference was significant (p = 0.0001). There was no significant difference of telomerase activity with respect to stage of tumor (p = 0.829), response to pre-operative chemotherapy (p= 1.0), tumor histology (p = 0.08), recurrence(p = 1.0) and overall survival ( p = 0.774).

Conclusion: Telomerase activity was found positive in 79% cases of wilms’ tumor. Telomerase activity was significantly more in the tumor tissue as compared to adjoining normal tissue (p = 0.0001), it could not be significantly correlated with stage of tumor, response to pre-operative chemotherapy, tumor histology, recurrence and overall survival.
INCIDENCE, TREATMENT AND OUTCOME OF RECURRENT (REC) MALIGNANT GERM CELL TUMORS (MGCT): A SINGLE INSTITUTION EXPERIENCE

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Aim: To evaluate the incidence and the outcome of treatment of recurrent (REC) malignant germ cell tumors (MGCT).

Materials and Methods: Prospectively maintained data of patients of MGCT managed in the pediatric solid tumor clinic from June 1994 through December 2016 was analyzed to evaluate the incidence of recurrence. Outcome was evaluated in terms of 5-year overall survival (OS) and disease free survival (DFS).

Results: Of the 152 MGCT cases (83 gonadal; 69 extragonadal)treated in this period, there were 49(32.2%) recurrences. 113 of 152(74.3%) were primarily treated by us and of these 18(15.9%) recurred. Thirty-nine(25.7%) were referred to us after resection and of these 31(79.5%)were with recurrence. The incidence of recurrence was similar among gonadal(27/83-32.5%) and extra-gonadal tumors(22/69-31.9%). The incidence of recurrence was maximum for testicular and least among the ovarian tumorts(Testicular: 53.3%; Sacrococcygeal:41.7% and ovarian:7.9%). The 5-year OS and RFS for the 152 patients was 0.9(95CI 0.83-0.94) and 0.61(95CI 0.52-0.69). Among the 49 REC-MGCT, 42(85.7%) were alive and 7(14.3%) had died giving a 5-year OS of 0.75(95CI 0.51-0.89). However, of these 42 survivors only 21(50%) were DFS, while the remaining 21 had progressive disease at last follow-up and chose to discontinue treatment. The 5-yr OS was 0.67 for extragonadal and 0.82 for gonadal recurrences (p=0.25). Of the 18 recurrences after primary treatment by us, 14 were alive (5-
yr OS 0.49) but only 3 were DFS. Among the 31 REC-MGCT referred after surgery elsewhere, 28 were alive (5-yr OS 0.89) and 18 achieved DFS.

**Conclusion:** The incidence of REC-MGCT was 32% and it was similar for gonadal and extra-gonadal tumors (32.5% vs 31.9%). Though the 5-year OS for REC-MGCT was 0.75, only 50% achieved DFS. The OS was better (0.89 vs 0.49) for patients who were operated elsewhere and came to us with recurrence (chemo naive patients) than our own patients (heavily pre-treated).