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Histiocytic Disorders H-1_V1.1

VALIDATION OF A SOLUBLE INTERLEUKIN-2 RECEPTOR ASSAY FOR THE DIAGNOSTIC OF HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS IN INDIAN CHILDREN

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Introduction: Hemophagocytic lymphohistiocytosis (HLH) is a cellular immune dysregulation caused by underlying genetic defects (Primary) or triggered by infection, malignancies or rheumatological conditions. Although raised soluble interleukin-2 receptor (sIL2-R, CD25) has been suggested as a biomarker, it is not routinely measured in India. The objective of the present study was to establish an assay and validate the cut-off value of sIL2-R for the diagnosis of HLH in Indian children.

Methods: Children with persistent fever, organomegaly, cytopenias with biochemical markers of HLH (fulfilling the criteria) were labeled as cases. Peripheral blood serum of cases and healthy was cry-opreserved. A double-sandwich enzyme immune assay was used to measure sIL2-R in a first batch of cases and controls. Standards and samples were run in duplicates. The optimum cutoff value was determined using ROC curve, and validated in a second batch of suspected HLH cases and controls.

Results: 74 children were enrolled (28 suspected HLH, 46 controls), with similar age/ sex distribution. The optimal sIL2R cutoff of 12ng/ml was found to be equivalent to 2400U/ml in the standardization batch (16 cases/ 22 controls). This cut-off in the validation batch (12 suspected cases and 24 controls) confirmed HLH in 11 cases, while it excluded HLH in 1 possible case. sIL2-R was higher in familial (n=8; median 4500U/ml [IQR: 3,305–4,183]) than HLH secondary to infective trigger, malignancy or SOJIA (n=19; median 4500U/ml [IQR: 3,305–4,183] vs. 2,810U/ml [1,655–3,720], p<0.001). On analyzing the prognostic significance of sIL2-R, sIL2-R \geq 3200U/ml was significantly associated with mortality (85.7% vs. 20.0% in patients with sIL2- R<3200, p=0.003).

Conclusion: A simple sIL2-R assay was successfully established. sIL2-R is higher in primary HLH and can aid in diagnosis and predict mortality especially when molecular diagnosis is delayed or not available. Normal age-related values of sIL2-R can be established in larger cohorts of healthy children.

Lymphoid Malignancies

LM-1_V1.1

FOLATE/VITAMIN B12 DEFICIENCY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA: BREAKING THE MYTH

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Background: Vitamin B12 & Folic acid (FA) supplementation in patients with a malignancy are considered counter-productive by making the cell stroma conducive to the proliferation of the malignant clone. Patients in lower middle income countries (LMIC's) have greater incidence of malnutrition with vitamin deficiencies. The need for refraining from supplementation of FA to patients with a malignancy in LMIC's has been questioned.

Aim: To evaluate the incidence of vitamin B12/FA deficiency in children on therapy for Acute Lymphoblastic Leukemia (ALL).

Materials & Methods: Children with ALL on therapy were randomly evaluated for serum B12 and folate levels. Serum B12 < 211pg/ml and serum Folate < 2 ng/ml were taken as deficient levels. Deficiency status was correlated to under-nutrition. Weight for age < -2z score was taken as under-nutrition (WHO).

Results: 85 children with mean age 6.8 yrs (6.03-7.73), including 50 on maintenance and 35 on induction/consolidation chemotherapy were evaluated.50 age and sex matched controls were also evaluated.

Induction/ Consolidation: 7/35 children (20%) were undernourished. Mean B12 levels were 330.4pg/ml (227.76-345.84), with 11 (32%) being B12 deficient. 2/11 patients were undernourished. Only1 child had folate deficiency, the mean levels being 8.55ng/ml (5.85-11.13).

Maintenance Therapy: 14 children (28%) were malnourished. Mean B12 levels were 500.56pg/ml (419.74-581.38). B12 deficiency was seen in 5 (10%) patients, with 3/5 being under-nourished. Mean Folate levels were 6.61ng/ml (5.56-7.66), deficiency being seen in 4 (8%) patients 3 of whom were under-nourished.

There was no difference of B12 & Folate levels when sex, T/B cell ALL, standard risk Vs high/intermediate risk ALL were compared. Undernourished children had significantly low levels of Folate (4.59 Vs 7.4; p=0.0139). This difference was not observed with B12 levels.

50 age/sex matched children taken as controls did not have either deficiency.

Conclusion: Under-nutrition in India is 45.9% as per National Family Health Survey (NFHS)-3 with reported prevalence of B12 & FA deficiency in the general population to be 7-33% and 20-33%; with a even higher prevalence in the undernourished. 25% of our cohort had under-nutrition. We had 5.8% with Folate & 20% children with B12 deficiency. Patients with co existing malnutrition had greater B12/FA deficiency. Higher B12 deficiency in induction/consolidation which may be due to higher demands or drug interactions needs further evaluation. A larger cohort would help conclude and nullify the hypothesis of FA supplementation to cancer patient in LMIC's. Under-nutrition in LMIC's remains the main issue to be tackled.

LM-1_V1.2

INVESTIGATING HEPATITIS B IMMUNITY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA PRESENTING AT A TERTIARY CANCER CARE CENTRE

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Background: Hepatitis B is a dreaded infectious disease and one of the major global public health problems and is the tenth leading cause of death. The global disease burden is staggering with about two billion people acutely infected and nearly 350 million chronically infected with hepatitis B virus (HBV). In India, the prevalence of hepatitis B surface antigen (HBsAg) among the general population ranges from 2% to 8%, placing India in an intermediate HBV endemicity zone. Our country has over 50 million cases making it the second largest global pool of chronic HBV infections. Waning of vaccine induced immunity leaves people at risk of acquiring hepatitis B infection in settings where the prevalence of infection is high. Vaccine- induced seroprotection (AntiHBs) is a useful surrogate of vaccine efficacy.

Objective: To assess immunity to Hepatitis B virus at initial presentation in children with newly diagnosed ALL treated in the Paediatric Oncology Division, Regional Cancer Centre, Thiruvanathapuram, Kerala.

Methods: Children (0-14 years) with newly diagnosed ALL treated between January 2016 to August 2016 were evaluated. Data regarding primary HB immunization were collected from the immunization card.AntiHBsAg titers were done at presentation using Enzyme Linked Fluoroscent Assay method using VIDAS (Bio-Merieux).Patients were classified as immune (antibody levels to hepatitis B surface antigen (antiHBs) >100mIU/ml), lowimmune (antiHBs10-100mIU/ml) and not immune (antiHBs<10 mIU/ml).

Results: Of the 109 children included (median age 5.6 years, M:F-1.5:1),75(68.8%) children had protective antiHBstitres (>10IU/L),34(31.2%) children had no immunity to hepatitis B.Of the 75 children with protective antiHBstitres 37 children (49.33%) had low immune antiHBstitres (10-100mIU/ml) and 38 children (50.66%) had immune antiHBstitres> 100 mIu/ml.Nopatients had active hepatitis B infection (hepatitis B surface antigenpositive) at presentation.

Discussion: Acute Lymphoblastic Leukemia (ALL) is the most common malignant disease in children. The more intensive treatment and risk stratification adopted over the last decade have resulted in an improvement in the survival rate, which, in many cases, reaches 90%. Both the illness and treatment affect the immune system. Immune competence