Confirmation of diagnosis in LAD-I requires demonstration of absence of CD18 and associated alpha subunit of CD11a, CD11b, CD11c on flow cytometry. 4 of 6 patients had complete absence of the integrins. Differential diagnosis include Interleukin-1 receptor associated kinase deficiency, Hyper IgE syndrome and leukemoid reaction. The only corrective treatment is hematopoietic stem cell transplantation. Reported survival in a largest series is5 years after follow up was 75%. These patients die in childhood if transplantation is not done and if the transplantation is carried out before serious infections, the prognosis is very good.
LAD is a rare form of congenital immune deficiency to be suspected in a child with delayed fall of umbilical cord, high WBC count with neutrophilia and consanguineous marriage. High index of suspicion and early diagnosis before infection sets in is important as mortality rate is high. Pseudomonas was most common organism isolated in the present study.

RBC Disorders

RBC-1_V1.1

ACQUIRED APLASTIC ANAEMIA IN CHILDREN – OPTIMAL OUTCOMES DEPEND ON OPTIMAL DELIVERY OF IMMUNOSUPPRESSIVE THERAPY

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Background: Acquired aplastic anemia (AA) is a haematological emergency in children and we have gained enormous knowledge about the pathogenesis and immune mediated self-destruction of stem cells and immunosuppressive therapy. Due to its rarity, we have limited data of this entity, especially, its course and outcome in resource limited countries.
Patients and methods: The case records of children who had been diagnosed to have AA since 2002 at our centre were reviewed. The diagnosis of AA was made in children with pancytopenia without organomegaly and confirmed by hypocellular bone marrow showing decreased expression of all three hematopoietic lineages. Clinical findings including dysmorphism, thumb abnormalities, congenital malformations and skin hyperpigmentation were noted down. Mitomycin C induced chromosomal instability to rule out Fanconi anaemia, Ham's test to look for paroxysmal nocturnal haemoglobinuria and chromosomal analysis to look for complex karyotypic abnormalities seen in myelodysplastic syndrome were documented in all patients.
After initial stabilization, the option of haematopoietic stem cell transplantation (HSCT) was offered to all those who had matched related donors. If not, immunosuppressive therapy was delivered within two months from diagnosis after the child was infection free. A combination of 40mg/kg/day of Horse derived antithymocyte globulin (ATGAM) and methylprednisolone at 2 mg/kg/day were started for the first 4 days through a central venous catheter. Oral cyclosporine and G-CSF were started on the fifth day and since 2015 Eltrombopag was added to the IST regimen. Revolade and GCSF were continued for about 8 to 12 weeks and cyclosporine from 6 to 12 months. All patient received Voriconazole and Acyclovir prophylaxis till neutrophil recovery to 1000.
Results: A total of 109 children had been diagnosed as AA, of whom, 42 had acquired AA. The mean age of children with acquired AA was 8.16 years (2-15 yrs). Boys were twice more commonly affected (ratio M: F = 2:1). Details are listed in table 1.
Of the 41, 21 underwent HSCT as they had fully matched related donor and 20 children received IST. Of the 20 children who received ATG, 10 children (70%) had complete remission in a median duration of 78 days. Two of the three non responders were treated with second IST and all three succumbed to the illness. One child developed acute myeloid leukaemia after achieving partial remission and was salvaged with HSCT, and 1 more non responder had an unrelated HSCT and is doing well. One child has suffered a relapse after a durable remission of over 18 months off immunosuppression. The 21 children who have been transplanted have an overall survival rate of 77 %.
Conclusion: Immunosuppressive regimen including Horse ATGAM, Methyl prednisolone, Cyclosporine, GCSF and Eltrombopag along with adequate and meticulous supportive care including neutropenic care, prompt infection management and the use of irradiated and leukodepleted blood products results in a 70% response rate and should be offered to all children with aplastic anaemia with no matched family donor. The addition of Elthrombopag has resulted in early recovery of all three cell lines and must be added to the IST protocol in children.

RBC-1_V1.2

DISCORDANT BEATS – A PROSPECTIVE STUDY OF CARDIAC MRI TO ASSESS IRON OVERLOAD IN PATIENTS WITH THALASSAEMIA MAJOR

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Introduction: Advances in blood banking has ensured optimal delivery of monthly transfusion needed to save the lives of about 10,000 new thalassaemia children born each year in our country. The burden of iron chelation has now increased as these children survive into their second and third decade of life. Cardiac failure secondary to myocardial haemosiderosis is the most common cause of mortality in these patients. Our study has been done to evaluate the prevalence and severity of cardiac ironload in children with beta thalassemia major and the effectiveness of serum ferritin as a marker of iron overload.
Patients and Methods: We conducted a prospective study from the year 2015-2016 where we performed T2* cardiac magnetic resonance (CMR), serum ferritin levels and pulmonary artery pressures by echocardiography in 100 patients with transfusion dependent beta thalassaemia major. The study had been approved by IRB at the VHS centre and informed consent was obtained from all of these families. The median age of our patients was 14 (range 7 TO 33 years) with 51% of them being female. The mean serum ferritin level was 2520.78 +-223.454 ng/ml. High iron overload with a serum ferritin of over 2500 was seen in 37% of our patients. The 29% patient group that had less than 1000 ferritin were considered to be chelated optimally as per international guidelines. A cardiac T2*of over 20 milliseconds was taken as a marker of heart free of iron overload.
The mean cardiac MRI T2* was 12.73 +-2.436 milliseconds. About 70% of our patients had moderate myocardial iron overload (T2* 10-20 ms) and 24% had severe iron overload (T2* <10ms). The mean pulmonary arterial pressure was 35.96+-8.3 mm of Hg. About 76% of the patients were on a single drug chelation therapy at the time of evaluation. Following the cardiac iron status they have been started on combination chelation therapy consisting of deferasirox and deferiprone.
We found no significant correlation (r=0.014, p=0.23) between the serum ferritin levels and myocardial ironload. The most significant finding was that 38 % (11/29) of our patients with serum ferritin < 1000 had severe cardiac iron load. A significant correlation could also be established between pulmonary arterial pressures and cardiac MRI T2 *(r=1.2, p =0.0024).

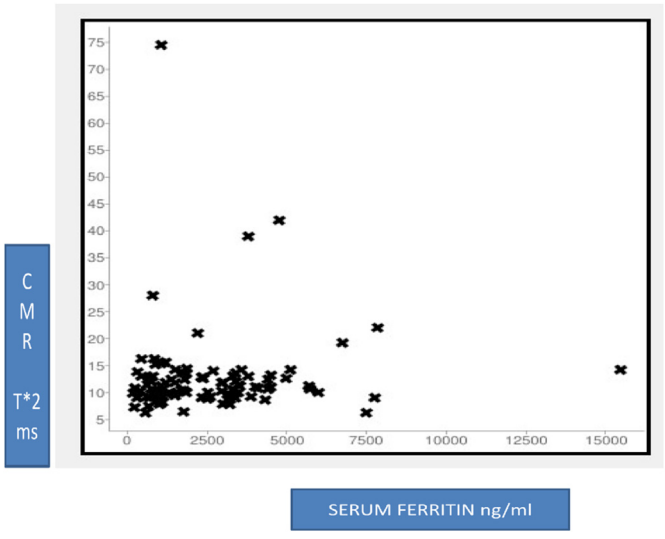

Figure 1. No correlation between serum ferritin and cardiac ironload.

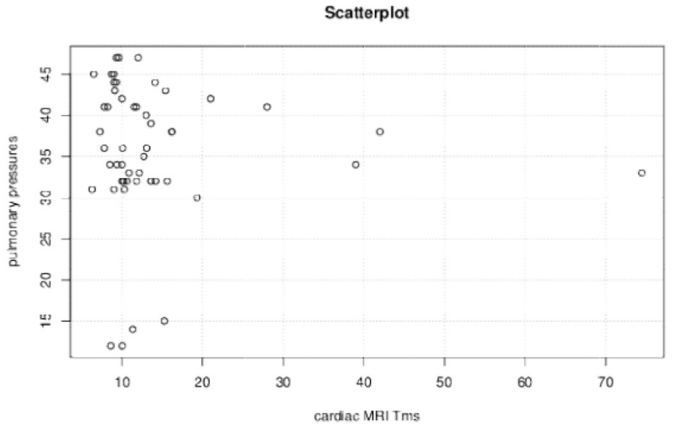

Figure. Significant correlation between pulmonary artery pressure and cardiac iron.

Conclusion: All patients with transfusion dependent thalassaemia major should be screened with a cardiac MRI for iron overload from the age of 7 years as serum ferritin done serially alone does not detect tissue iron deposition. Aggressive chelation with the addition of deferiprone which acts synergistically with deferasirox or desferrioxamine must be commenced to reduce the incidence of cardiomyopathy in these patients despite a low serum ferritin value. This is the first comprehensive study of cardiac iron in India and we plan to follow up this cohort annually to evaluate the outcome of the intervention with serial cardiac MRI.

RBC-1_V1.3
A PROSPECTIVE OBSERVATIONAL STUDY ON CLINICO-ETIOLOGICAL PROFILE OF PANCYTOPENIA IN CHILDREN

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Background: Pancytopenia is a disorder in which all three major formed elements of blood (red blood cells, white blood cells and platelets) are decreased in number.Relevance of the study lies in the timely intervention for the causes of pancytopenia which can either bring about a complete cure or at least a remission from the disease entity. In India not many studies have been done on this topic especially in pediatric age group so the present study has been undertaken to evaluate the various causes of pancytopenia, their clinical profile and outcome.
Methods: This was a prospective observational study of 81 patients aged between 1 month to 15 years admitted to Department of Pediatrics of King George Medical University, Lucknow during August 2015 to July 2016 with Hb<10g/dl, TLC<4000/mm^3 and platelets<1 lakh/mm^3. Patients undergoing/already undergone chemotherapy and radiotherapy were excluded.After informed consent, a detailed medical history, physical examination, complete blood counts, anaemia workup, viral markers, bone marrow examination was done along with transfusion records, treatment received and outcomes were analysed.
Results: The bulk of patients were from rural background (87%).The mean age at presentation was 74 months (range 1-180 month) with Male:Female – 2.8:1.
The most common clinical presentations were fever (78%), pallor (67%), bleeding manifestations (43%); past h/o jaundice (5%) and pesticide exposure (8%); hepatomegaly (56%) splenomegaly (42%) Lymphadenopathy (22%) and knuckle hyperpigmentation (14%).
The haematological parameters showed mean haemoglobin level: 4.9 gm/dL, WBC: 2676/mm^3, ANC: 1009/mm^3, platelet: 43700/mm3, MCV:85.5 MCH: 30.5 RDW: 23.5 B12 487.7 Folate 12.3 Ferritin 777 s.Iron 179.8 .PNH clone was present in 2.1%, Parvo B19 in 6% and EBV in 7% of patients.
5 patients (6%) were lost to follow up or expired before any treatment was initiated.
Most common causes of pancytopenia found in our study were Aplastic Anemia (49%), Acute leukemia (27%) and Megaloblastic/Nutritional (18%). Infections (9%) and hypersplenism (6%) etc accounted for the rest.
All patients with megaloblastic anemia survived despite no transfusions. But patients with very severe Aplastic Anemia and hematological malignancies had worse outcomes despite ATG courses ; multiple transfusions and induction chemotherapy respectively.Patient with Kala Azar, chronic Malaria infections and hypersplenism survived after appropriate treatment.Also hospital stay was prolonged for leukemias and Aplastic Anemia.
Conclusion: The etiology of pancytopenia varies widely ranging from transient marrow viral suppression, drugs etc to marrow infiltration by life-threatening malignancy.The severity of pancytopenia and the underlying pathology determine the management and prognosis of the patients .Hence such studies will help in planning the diagnostic and therapeutic approach in patients with pancytopenia and curtailing delays to reduce multiple transfusions, pre-treatment infections and overall morbidity and mortality associated with entity of Pancytopenia.

RBC-1_V1.5
ADVERSE DRUG EVENTS WITH IRON CHELATION DRUGS IN THALASSEMIC PATIENTS ATTENDING A DAY CARE THALASSEMIA CENTRE IN TERTIARY CARE GOVT. MEDICAL COLLEGE IN NORTH INDIA

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Introduction: The Last three decades have witnessed profound changes in the management of patients with thalassemia major. Regular and periodic blood transfusion being the main stay of treatment results in iron overload thus necessitating need for iron chelation. At present three iron chelators namely, Desferrioxamine, Defriprone and defirasirox are in use alone or in combinations. Since the iron chelators are required to be given for the lifetime they also cause adverse events which are range from trivial to life threatening.
Aims: To identify and manage adverse drug events due to iron chelating drugs experienced by thalassemic patients.
Material and methods: This is an observational study done during 1st January to 30th June 2016 in Thalassemia Day Care Centre of SMGS hospital, Govt. Medical College Jammu. All the adverse events were recorded on a pretested proforma and were validated on Naranjo causality assessment scale.
Results: Of the 280 patients with the age ranging from 6 months to 53 years registered with Thalassemia Day Care Centre SMGS hospital Govt. Medical College Jammu only 180 attended regular fortnightly follow up clinics. Out of these 180 patients 168 are on Iron chelation drugs (129 on Defriprone, 24 on Defirasirox, 8 on Defriprone + Desferrioxamine, 4 on Desferrioxamine and 3 on Defriprone + Desferrixamin) Out of 32 events observed during the course of study 21 (65.62%) were due to Defriprone, 8 (25%) due to Deferasirox and 3 (9.38%) due to Desfferioxamine. Out of 21 events due to Defriprone 12 (57.14%) were gastrointestinal symptoms, 5 (23.8%) arthropathy, 2 (9.5%) Neutropenia and 2 (9.5%) thrombocytopenia. All 8 (100%) events due to Deferasirox were gastrointestinal symptoms. 2 (66.66%) events with desferrioxamine were local reactions and 1 (33.33%) was encephalitis. On Naranjo Casuality scale 5/32 was definite while as 24 /32 was probable and 3/32 were possible. While 9 were mild reactions, 4 were severe reactions and 19 were moderate reactions.
Conclusion: Majority of adverse events were observed with Defriprone followed by Deferasirox. Although least adverse events were observed with desferrioxamine, but adverse events with deferasirox were least severe.
Keywords: Adverse drug events, Iron chelation, Thalassemia

RBC-1_V1.6
ACQUIRED APLASTIC ANAEMIA IN CHILDREN – OPTIMAL OUTCOMES DEPEND ON OPTIMAL DELIVERY OF IMMUNOSUPPRESSIVE THERAPY

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