single-center review from Kortsalioudaki, *et al*. [3] which affirmed its beneficial effect in acute liver failure. Based on these data, the consensus among pediatric hepatologists over the years has been to use this inexpensive medication in liver failure.

However, a recently published, decade long, multi-centric, randomized placebo controlled study to test the widespread assumption of usefulness of intravenous NAC in non-acetaminophen pediatric liver failure by Squires, *et al*. [4] does not support broad use of NAC in this condition. The study by Squires, *et al*. in itself is unique with regard to its design and the results and perhaps is the only prospective study in children which tries to give an insight to the role of NAC in non-acetaminophen pediatric liver failure. More prospective studies are still warranted before we can establish the role of NAC in treatment of non-acetaminophen pediatric acute liver failure.

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REFERENCES

1. Bhatia V, Bavdekar A, Yachha SK. Management of acute liver failure in infants and children: Consensus Statement of the Pediatric Gastroenterology Chapter, Indian Academy of Pediatrics. Indian Pediatr. 2013;50;477-82.
2. Harrison PM, Wendon JA, Gimson AE, Alexander GJ, Williams R. Improvement by acetylcysteine of hemodynamics and oxygen transportin fulminant hepatic failure. N Engl J Med. 1991;324:1852-7.
3. Kortsalioudaki C, Taylor RM, Cheeseman P, Bansal S, Mieli-Vergani G, Dhawan A. Safety and efficacy of N-acetylcysteine in children with nonacetaminophen-induced acute liver failure. Liver Transpl. 2008;14:25-30.
4. Squires RH, Dhawan A, Alonso E, Narkewicz MR, Shneider BL, Rodriguez-Baez N, *et al*. Intravenous N-acetylcysteine in pediatric patients with nonacetaminophen acute liver failure: A placebo-controlled clinical trial. Hepatology. 2013;57:1542-9.

Reversible Skin Hyperpigmentation in Imerslund-Grasbeck Syndrome

A 2-year-old girl presented with progressive hyperpigmentation of both the distal interphalangeal joints of fingers and toes along with palmar and plantar hyperpigmentation of both hands and feet for the last one year with no other associated symptoms. Clinically, her weight (13.5 kg), height (91 cm) and developmental assessment were appropriate for age. Her other systemic examination but for her skin pigmentation were all normal. Investigations were not contributory, other then a low vitamin B_{12} level (84.2 pg/mL) and mild megaloblastic picture in bone marrow. A diagnosis of Imerslund-Grasbeck syndrome (IGS) was considered and was treated with intramuscular injection of 1000 µg methylcobalamin daily for 7 days, followed by weekly injections for 1 month and then oral doses of 1000 µg daily. With therapy, there was a significant change in 10 days time and there was total resolution of skin lesion in a month's time. She was advised to have lifelong daily therapy with 1000 µg oral methylcobalamin.

Hyperpigmentation due to vitamin B_{12} deficiency appears only in patients whose skin is normally pigmented, hence may not be a feature in Caucasians, whereas it is more common in darker-skinned patients. In Indian children, isolated mucocutaneous lesions could be one of the earliest signs of B_{12} deficiency [1] that may predate other systemic manifestations. IGS should be considered in any individual with macrocytic anemia, reduced serum B_{12} levels and proteinuria. This child with IGS had only skin manifestation on presentation, probably with time haematological manifestations could have surfaced, as evidenced by the marrow revealing megaloblastic changes despite other haematological indices being normal. Life-long treatment with vitamin B_{12} is necessary for IGS, which alleviates hematologic, gastrointestinal and CNS symptoms except proteinuria [2]. High oral doses of B_{12} (1000 µg and 2000 µg) is safe, acceptable and as effective as intramuscular administration [3,4]. Oral treatment is based on the finding that in larger doses, sufficient amounts are absorbed even in the absence of intrinsic factor.

Available literature suggests that, pigmentary changes remain unresponsive with vitamin B_{12} replacement in IGS as was observed in two Chinese siblings [5]. This child with vitamin B_{12} replacement had complete resolution of skin pigmentation but her proteinuria persisted even on follow up for 3 years.

To conclude, a diagnosis of vitamin B_{12} deficiency has to be considered in any case of isolated skin hyperpigmentation.

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REFERENCES

1. Jadhav M., Webb JK, Vaishnava S, Baker SJ. Vitamin B12 deficiency in Indian infants. A clinical syndrome. Lancet. 1962;2:903-7.
2. Grasbeck R., Tanner SM. Juvenile selective vitamin B12 malabsorption: 50 years after its description – 10 years of genetic testing. Pediatr Res. 2011;70:222-8
3. Nyholm E, Turpin P, Swain D, Cunningham B, Daly S, Nightingale P, *et al*. Oral vitamin B12 can change our practice. Postgrad Med J. 2003;79:218-20.
4. Vidal-Alaball J, Butler CC, Cannings-John R, Goringe A, Hood K, McCaddon A, *et al*. Oral vitamin B12 versus intramuscular vitamin B12 for vitamin B12 deficiency. Cochrane Database Syst Rev CD004655 (2005). doi:10.1002/14651858.CD004655.pub2
5. Lin SH, Sourial NA, Lu KC, Hsueh EJ. Imerslund-Grasbeck syndrome in a Chinese family with distinct skin lesions refractory to vitamin B_{12}. J Clin Pathol. 1994;47:956-8.

Status of Primary Immunodeficiency Disorders in India

We read the recent article on approach to primary immunodeficiency disorders (PID) [1] with interest. These disorders are under-diagnosed in the developing world. On reviewing published Indian data on PID we came across only 4 large series reporting a total of 386 cases [3-5]. Most common PID's reported are disorders of immune dysregulation followed by phagocytic disorders and predominant antibody deficiencies [4,5]. High mortality rates of upto 51% have been reported [5].

We report here a series of 11 children (8 males) registered in our PID clinic from January to July 2013. Eight were males and three females. Mean age was 5.2 years (4 months-12 yrs.). Two had *X*-linked agammaglobuinemia. Both are on replacement intravenous immunoglobulin (IVIG) therapy and doing well. Third, a 12-year-old male presented to us with severe aplastic anemia (SAA) with common variable immunodeficiency. He underwent matched sibling donor bone marrow transplant (BMT) for SAA. At eighty days post-transplant, he has normal blood counts and immunoglobulin levels. Fourth child had pure red cell aplasia with isolated IgM deficiency. He responded well to prednisolone. Fifth child had congenital neutropenia and negative for ELANE mutation for congenital neutropenia. His neutrophils increased only after high dose granulocyte colony stimulating factor (60 ug/kg/day). Sixth patient had hemophagocytic lympho histiocytosis and was managed as per HLH 2004 protocol. Two infants were diagnosed as cases of autoimmune lymphoproliferative syndrome and are doing well on prednisolone and mycophenolate. Two were diagnosed as case of Heme-oxygenase-1 deficiency with auto-inflammatory syndrome. One boy was diagnosed with *X*-linked severe combined immunodeficiency and underwent matched unrelated donor BMT abroad without conditioning. Although his T-cells and NK-cells recovered but he still has low immunoglobulin levels.

Our small series shows that improvement in survival is possible; although, pan-India improvement would require increased awareness among pediatricians, establishing specific centers offering genetic diagnosis and definitive therapy like BMT.

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REFERENCES

1. Madkaikar M, Mishra A, Ghosh K. Diagnostic approach to primary immunodeficiency disorders. Indian Pediatrics. 2013; 50: 579-586.
2. Verma S, Sharma PK, Sivanandan S, Rana N, Saini S, Lodha R, *et al*. Spectrum of primary immune deficiency at a tertiary care hospital. Indian J Pediatr. 2008; 75:143-148.
3. Gupta S, Madkaikar M, Singh S, Sehgal S. Primary immunodeficiencies in India: a perspective. Ann N YAcad Sci. 2012; 1250:73-79.
4. Madkaikar M, Mishra A, Desai M, Gupta M, Mhatre S, Ghosh K. Comprehensive report of primary immunodeficiency disorders from a tertiary care center in India. J Clin Immunol. 2013; 33(3):507-512.
5. Chinnabhandar V, Yadav SP, Kaul D, Verma IC, Sachdeva A. Primary Immunodeficiency Disorders in the Developing World: Data from A Hospital-Based Registry in India. Pediatric Hematology and Oncology.2013 June12 (Epub ahead of print) (doi:10.3109/08880018.2013.805346)