Inborn errors of immunity or primary immune deficiency disorders (PIDDs) occur with a frequency of 1 in 5000 to 1 in 1000 [1], and are frequently misdiagnosed resulting in avoidable morbidity and mortality [2]. Diagnostic tests and hematopoietic stem cell transplants (HSCT) are not uniformly accessible [3].

Government Medical College, Kozhikode, a tertiary care hospital in Kerala, and CSIR Institute of Genomics and Integrative Biology, Delhi have been conducting a program on primary immune deficiency disorders over the last five years. Although HSCT is often the only curative option, we are dependent on centers outside the state. The study was designed to document the clinical characteristics of children who underwent HSCT for an inborn error of immunity.

Hospital records of children with PIDDs who attended the immune deficiency clinic from June, 2015 to May, 2020 were obtained and data of those who underwent HSCT were analyzed. Only children who had completed at least 3 months post-HSCT were included. Variables studied included age at onset diagnosis and at HSCT, gender, relationship with stem cell donor, time since HSCT and diagnostic genetic or phenotypic marker. Quantitative variables were entered on an Excel data sheet and frequency and associations calculated using the statistical package Epi Info (version 7.2.3.1).

HSCT was performed in 13/67 (19.4%, 11 boys). The indications included Wiskott-Aldrich syndrome (4, 30.8%), and leukocyte adhesion deficiency, severe combined immune deficiency, and X-linked agammaglobulinemia in two each (15.4%) congenital neutropenia Fanconi anemia, and hyper IgM syndrome were diagnosed in one child each. The median (IQR) age at diagnosis of children who underwent HSCT was 14 months (first quartile, III quartile). The median (IQR) age at HSCT was 27.5 (first quartile, III quartile) months and the median (IQR) interval between diagnosis and HSCT was 7 (first quartile, III quartile) months. Recurrent pneumonia was the commonest presenting feature in 7 (54%) children, followed by frequent skin and soft tissue infections in 6 (46%) and recurrent otitis media in 4 (30.8%). Frequent abscesses, recurrent diarrhea and bleeding were presenting features in 2 (15%) children each. HSCT was done in an asymptomatic child with Fanconi anemia after his elder sister succumbed to the same disease.

Of the 13 children who underwent HSCT, 9 (69%) children had a matched sibling donor and 2 children each (15%) had matched unrelated donor transplants (MUDs) [4] and haploidential stem cell transplants. Reduced intensity conditioning (RIC) [5] with treosulfan and fludarabine was used.

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Hematopoietic Stem Cell Transplantation for Children With Inborn Errors of Immunity

This is a retrospective analysis of clinical characteristics of children with inborn errors of immunity who underwent hematopoietic stem cell transplant (HSCT). Although the mean age at diagnosis was 24.4 months, it was 51.9 months at HSCT. There is an urgent need to improve awareness, expand donor registries and initiate newborn screening for inborn errors or immunity.

Key words: Primary immune deficiency disorders.
used and 12 children had sustained engraftment. There was one graft rejection with autologous reconstitution, and a second HSCT resulted in sustained engraftment. Post-HSCT complications included bacterial sepsis, cytomegaloviral reactivation, steroid-induced hypertension and graft versus host disease. There was no mortality and the mean duration of post-transplant event-free survival was 25.1 months.

HSCT was performed for 2 (15%) children with XLA. Although this is not the standard treatment, it has been found to be a feasible option where availability and cost of immunoglobulin replacement therapy are limiting factors and parents are not keen on lifelong replacement [6].

The median interval between onset of symptoms to diagnosis was 9 months. This emphasizes the need to improve awareness among pediatricians [2]. The mean interval between diagnosis and HSCT was 40.9 months, accounting for the high mortality. Improved outcomes are described with HSCT before diagnosis and HSCT was 40.9 months, accounting for the high mortality. 

The outcome of HSCT for children with matched unrelated donors (MUDs) and haploidentical donors has improved globally [4,9] both children in this series had good outcomes. Limitations of the study include the small sample size and the variable time since HSCT with possible recall bias.

The main stumbling blocks to wider use of HSCT remain the cost and non-availability of suitable donors. National rare disease policy addressing the major concerns of affected families would be the way forward. Awareness regarding PIDDs should be rapidly scaled up, donor registries expanded and government funding streamlined. A newborn screening program would help to reduce mortality.

Acknowledgements: Dr. Dhanasooraj, Scientist, MRU, Govt. Medical College, Kozhikode, Dr. Ajith Kumar VT and Dr. MP Jayakrishnan, Department of Pediatrics, Government Medical College, Kozhikode, Athulya EP, Junior Research Fellow, and Ablunev Jain and Dr. Sindhar Sriyambbu at the CSIR - Institute of Genomics and Integrative Biology, Delhi.


Contributors: GMG: conceptualization of the study, data analysis and writing the paper. RR and RU oversaw the work-up and procedure for HSCT, VS: did the genetic work up for the patient. All authors approved the final draft of the paper.

Funding: Science and Engineering Research Board, Delhi, and Foundation for Primary Immune Deficiency Diseases (FPID); Competing interest: None stated.

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Indian Pediatrics 180 Volume 58—February 15, 2021