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Acute childhood leukemia in India: Where are we going, where have we been?

Arora and Arora[1] have done an excellent job of surveying the landscape of childhood acute leukemias as it exists in India over the last two decades. Their findings are not novel, but the review highlights several important points:

First, they once again emphasize that studies providing outcomes data in India as it relates to childhood leukemia are primarily hospital-based (eight for acute lymphocytic leukemia [ALL] and five for acute myeloid leukemia [AML]). Only two population-based studies were found, (one each for ALL and AML). Despite the love that cancer control experts have for population-based cancer registries, these tools are resource intensive and hard to implement in Indian conditions. Outcomes data collected by a hospital-based cancer registry (HBCR) are more cost effective, and since the International Society for Pediatric Oncology (SIOP) recommends childhood cancer care be provided by a multidisciplinary pediatric cancer unit (PCU), the PCU-based cancer registry serves as the pediatric component of the HBCR. Utilizing technology such as web-based systems has further improved data collection, and both St. Jude Children's Research Hospital (Pediatric Oncology Network Database) and the Jiv Daya Foundation (IndiaPOD Database) use such technology. The PCU-based registry has proven to be an effective, low-cost solution for data gathering and has the added advantage of allowing all the stakeholders in patient care (oncologists, social workers, data managers) to work together to improve patient outcomes in real time.[2]

Second, although an estimated 3761 children with ALL and 361 children with AML were reviewed, the authors correctly emphasize this is a fraction of the patients expected over a 10-year period, once again drawing attention to the fact that refusal or abandonment of treatment has been a major cause of therapeutic failure in childhood cancer in India. The majority of the study data is before 2010, when SIOP finally established a working group to address abandonment. They defined it as failure to either begin (previously termed refusal), or a break of >4 weeks, in planned curative treatment. It should be always be documented as an adverse event and not just censored from cancer survival data, and results from socioeconomic factors beyond the control of the patients and parents, who should not be blamed. Addressing abandonment is a multifactorial task and requires efforts from a variety of stakeholders. For example, advocacy groups such as "Can kids … Kids can" provide an array of services to pediatric oncology patients seeking treatment, with financial assistance, social work support, a "home away from home," and actively collaborate with over 34 children's cancer hospitals throughout India to help reduce abandonment.

Third, toxic deaths in ALL were significant and ranged from 2%-13% during induction and 4%-24% during treatment. The 13% induction mortality seen in ALL, is over ten times the rate in better-resourced countries, and in AML the induction mortality was even higher at 25%. Such morbidity negatively impacts childhood cancer outcomes in several ways. For example, in centers where the majority of patients die from toxicity, parents may choose to abandon therapy, and caregivers may refuse offer potentially curative therapy. At a broader level, community and childhood cancer advocates may hesitate to commit resources to a condition where the majority of patients die after receiving treatment. Improved supportive care helps not just children with acute leukemia, but many other acute conditions, and is one of the areas where the investment of resources may help children across multiple subspecialties.[3]

Finally, the majority of patients were treated on protocols that would currently be considered sub-standard. Protocols such as MCP 841 were state of the art in the 1970s, and made available at a time when there was uncertainty that children with ALL in India could be successfully treated with chemotherapy. The fact that patients who received and completed therapy on MCP 841 achieved an overall survival of 45–81% and event-free survival of 41–70% was in itself remarkable, and the impact of such results was to create a generation of pediatric oncologists who realized that childhood leukemia in India was treatable and curable. The time has now come to further improve survival by creating protocols for Indian conditions updated to incorporate the latest treatment principles. For example, the authors correctly emphasize that the Indian Pediatric Oncology Group (InPOG) recently commenced the InPOG-ALL-15-01 clinical trial, using minimal residual disease to improve risk stratification, and we hope and expect to see many such collaborative trials over the next few years. There still remains a need to follow the survivors of earlier generation protocols for the late effects of interventions such as cranial radiation, where secondary cancers may manifest several decades later.

In summary, curing childhood leukemia is a team effort, and we have confidence that thanks to the hard work by all the stakeholders involved in the care of childhood acute leukemia in India, when we look back in 2020, we will find survival rates and other metrics markedly improved compared to the numbers Arora and Arora have presented us with.

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