Article published online: 2021-08-06



# Multidrug Resistant Infections in Paediatric AML: An Ominous Sign of the Times to Come

Suvir Singh[1], Kunal Jain[2] Jagdeep Singh[2] Davinder Paul[2]

[1]Department of Clinical Hematology, Dayanand Medical College and Hospital, Ludhiana, Punjab, India
[2]Department of Medical Oncology, Dayanand Medical College and Hospital, Ludhiana, Punjab, India

**Address for correspondence** Suvir Singh, MD, DM, Department of Clinical Hematology & Bone Marrow Transplantation, Dayanand Medical College and Hospital, Ludhiana, Punjab, 141001, India (e-mail: suvirs@gmail.com).

Ind J Med Paediatr Oncol 2021;42:213–214.

Uppuluri et al recently reported a single center experience with management of pediatric acute myeloid leukemia (AML) and impact of infectious complications over a two-decade period.[1] This is a highly informative study and allows inference of chronological trends in etiology of infectious complications and mortality in pediatric AML across India. It is commendable to note that despite an increase in the prevalence of multidrug resistant (MDR) organisms, early infection-related mortality of less than 10% was achieved. We highlight three other pertinent conclusions that must be drawn from this study and have wider implications.

The finding of *Klebsiella pneumoniae* as the most common Gram-negative pathogen is in line with several other Indian studies on AML.[2] Alarmingly, the incidence of MDR bacteremia in Indian data continues to increase, with one study noting carbapenem resistance in 60% and colistin resistance in 80% of isolates.[3] An increasing trend in MDR Gram-negative infections after 2012 is echoed in the same study, rising from 0% before 2012 to over 20% in 2017. This has shown exponential rise in the use of colistin, tigecycline, and carbapenems. Despite a rise in MDR infections, the new antibiotic pipeline (including agents in all phases of development) as of 2019 has been found to be similar to the one in 2013 and 2015, indicating an unavoidable lag between emergence of resistant isolates and identification of newer agents.[4]

This trend is foreseen to cause greater challenges in the coming few years, and must be mitigated with steps taken today. First, implementation of antibiotic stewardship programs has been shown to reduce broad-spectrum antibiotic usage in the absence of clinical or microbiologic indications and must be implemented where possible. For instance, pharmacy guidelines that prevent the use of carbapenems without definite indications potentially reduce unnecessary antibiotic usage. The use of stool surveillance, as used by the authors, allows risk-adapted initiation of carbapenems/colistin/tigecycline in appropriate patients and has reduced unnecessary antibiotic usage. Neutropenic patients with AML usually need to be started on broad-spectrum antibiotics agents in the absence of microbiologic proof. Active antibiotic deescalation in AML, guided by microbiology reports, allows a reduction in broad-spectrum antibiotic usage without affecting clinical outcomes and must be followed wherever possible.[5]

Fungal infections constitute the next biggest threat to patients with acute leukemia. Posaconazole provides effective antimold activity and is the agent of choice for most patients with AML. The authors report low rates of proven fungal infections, with the use of micafungin for all patients. Micafungin has demonstrated reduced rates of prophylaxis failure in patients with AML, but it is associated with a similar incidence of invasive fungal infections and a higher incidence of infections with uncommon species like *Mucoralres*.[6] Several problems associated with posaconazole such as drug interactions, variable absorption, and peak drug levels are overcome with micafungin, and a decision to switch must be taken based on individual data.

It is again impressive to note that the induction mortality despite high rates of MDR infections has largely stayed around the 10% mark. Cognizant use of broad-spectrum antibiotics, directed by clinical and microbiologic indications, is essential to prevent the emergence of an MDR Gram-negative pandemic in the coming years.

**Author Contributions**

SS and KJ conceptualized the paper. SS wrote the article. SS, KJ, JS, and DP contributed to literature search and reviewed the final manuscript.

The manuscript has been read and approved by all the authors. The requirements for authorship, as stated earlier

**DOI** https://doi.org/10.1055/s-0041-1731842
**ISSN** 0971-5851

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in this document, have been met, and each author believes that the manuscript represents honest work.

**Conflict of Interest**
None declared.

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