

Dilemma in Diagnosis and Management of CML in Pakistan

Khan S. et al.: Dilemma in Diagnosis and Management of CML in Pakistan

Sahrish Khan¹, Muhammad Farooq Sabar^{1,2}, Mariyam Akbar³, Abdul Waris⁴

¹University of the Punjab, Center for Applied Molecular Biology (CAMB), Lahore, Pakistan

²University of the Punjab, School of Biochemistry and Biotechnology, Lahore, Pakistan

³Mayo Hospital, Department of Oncology, Lahore, Pakistan

⁴City University of Hong Kong, Department of Biomedical Sciences, Hong Kong SAR

Muhammad Farooq Sabar, M.D., University of the Punjab, Center for Applied Molecular Biology (CAMB);
University of the Punjab, School of Biochemistry and Biotechnology, Lahore, Pakistan
farooq.camb@pu.edu.pk

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Dear Editor,

The BCR-ABL fusion genes cause chronic myeloid leukemia, leading to the abnormal activation of the ABL1 kinase and enhancing leukemic cell proliferation. CML patients categorized into three phases: chronic, accelerated, and blast phase [1]. Several biomarkers were employed in diagnosing and confirming the disease. CML can be effectively controlled by adopting tyrosine kinase inhibitors (TKIs) [2]. Pakistan ranks as the fifth largest country in the world with more than 240 million population and classified as a middle-income nation. The majority of patients were from Punjab (67.6%) and Khyber Pakhtunkhwa (20.2%), including rural and urban areas of these provinces [3]. CML, being a somatic cancer, involves various environmental, nutritional, and genetic factors.

Despite notable advancements in the treatment of CML in recent years, imatinib remains the primary therapy initially utilized, acting to inhibit the oncoprotein. Second-generation TKIs like nilotinib offer increased effectiveness compared to imatinib, targeting a broader array of pathways. In cases of imatinib resistance, patients often transition to nilotinib. However, for those resistant to nilotinib, ponatinib emerges as a preferred strategy. Nevertheless, the effectiveness of TKIs is limited, and managing blast crisis (BC) remains a formidable challenge in CML treatment. In this progressed stage of the disease, there is an evidence of a complex mix of clonal, genomic, and molecular variations, frequently involving additional abnormalities in chromosomes and mutations within the BCR::ABL1 kinase domain, as well as other genes associated with leukemia. For patients failing multiple TKIs, including third-generation ponatinib, outcomes remain unsatisfactory with limited treatment options available [4]. In addition, managing the disease in older individuals, pregnant women, TKIs resistant patients, and those with comorbidities present additional hurdles in both diagnosis and treatment. This complexity often leads to adverse outcomes, with mortality being a frequent consequence.

Difficulties are encountered in both the management and diagnosis of CML. The Pakistani government provides access to Imatinib and Nilotinib, but third-generation TKIs are not widely available. The primary obstacle lies in the cost of diagnostic tests, which are crucial for CML patients. Hematological, cytogenetic, and molecular tests recommended to assess the disease status. Additionally, a fresh complete blood count (CBC) test is conducted at each follow-up appointment. Some patients show resistance, and a mutational analysis test is recommended which involves advanced techniques like Next generation sequencing, whole exome sequencing, Sangar sequencing or panel sequencing must be performed to evaluate the changes in the genome, and the best strategy for therapy would be planned. However, these tests are too costly for middle-class people to afford as each test costs more than half of a laborer's monthly income. Furthermore, the government of Pakistan does not provide testing facilities.

There are few oncology departments in government hospitals. Pakistan Atomic Energy Commission (PAEC) has 19 PAEC-managed Atomic Energy Cancer Hospitals (AECHs) spread across the country, significantly contributing to alleviating the cancer burden in the country and handling almost 80% of cancer cases in Pakistan [5]. Timely improvement in the diagnosis and management of CML is a pressing issue in Pakistan. The government of Pakistan should take measures to establish cancer care hospitals in every district of the country. Diagnostic facilities and

genetic screening should be available in hospitals. Facilities for third-generation, advanced TKIs and combination therapies should be provided to enhance treatment options and improve patient outcomes.

Keywords: Chronic Myeloid Leukemia, TKIs Resistance, CML Management, CML Diagnostic Advance Techniques, CML Therapies in Pakistan.

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