

Cytotoxic Therapy of Colorectal Carcinoma in Pakistan

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Colorectal carcinoma (CRC) is associated with highest cancer mortality rate next to lung carcinoma.¹ Cancer statistical report by WHO in Pakistan indicate that colorectal carcinoma is the predominant cause of cancer mortality ranking seventh in women and eighth in men². Colorectal cancer patients in Pakistan are presented with distinct clinical features e.g. subsided lesions, comparatively young age and rapidly progressive advanced cancer stage with multiple sites of distant metastases. These features substantially contribute to surgical complications and assign severity to the toxic profile of cancer chemotherapy. Early diagnosis of CRC, which is otherwise a slow developing cancer, reduces the aforementioned added complications with cancer treatment. Multiple factors like inappropriate and incorrect awareness, socioeconomic strain and inadequate health care facilities prevent early diagnosis of the disease.³ Screening for CRC is both complex and challenging in populations with economic instability and high incidence rate due to lack of factors like risk stratification, patient's acceptance, adequate financial insurance, appropriate diagnosis, treatment and follow up.⁴

Colorectal carcinoma rarely arises from genetic polyposis syndrome, whereas, the usual source of origin is familial adenomatous polyposis, caused by APC (adenomatous polyposis coli) gene mutations or sporadic adenoma. Fecal blood can be detected in colorectal cancer patients by occult blood tests, stool test and fecal DNA tests even before any apparent clinical symptom. Endoscopic screening e.g. flexible sigmoidoscopy or colonoscopy helps in the detection, removal and biopsy of the polyps and thus referred to as gold standard diagnostic procedures.⁵

5-FU synthesized by Heidelberger in 1975, remains to be the most effective drug administered in different combination schedules, dosages and routes for the treatment of colorectal carcinoma. The first line therapy for untreated metastatic CRC is bevacizumab in combination with 5Fluorouracil, Leucovorin and Irinotecan (FOLFIRI).⁶ Affordability of treatment is a major hindrance in provision of standard therapeutic option to most patients in Pakistan, who are solely treated with 5Fluorouracil and Leucovorin in adjuvant settings.

The study reported by Bano *and colleagues*⁷ in this

issue, discusses cardiac toxicity induced by different schedules of FOLFOX in patients of colorectal carcinoma. Effects on cardiac enzymes and serum biomarkers are indicative of substantial risk of adverse cardiac events in susceptible patients. Estimated risk of delayed cardiovascular adverse effects in this study needs to be further verified in patients previously treated with FOLFOX schedule in follow-up routine with objective clinical investigations. The clinical study however signifies the "need to train a generation of cardio-oncologist or onco-cardiologist"⁸ for management of cardiac toxicity with successful estimates in cancer patients, by definition of personalized cytotoxic therapy.

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