Carcinoma Gallbladder- an Indian Problem

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Gallbladder cancer is an uncommon cancer worldwide, but one of the commonest cancer in North India. Apart from India, it is common in South America and Japan. The disease is characterized by late onset of symptoms, advanced stage at presentations and a rapidly progressive disease with a median survival of 6 months in advanced disease [1].

Epidemiological studies have been few and it is difficult to draw much meaningful conclusions from these studies. The etiological factors contributing to the development of this disease still remains to be elucidated. Numerous risk factors- female sex, high BMI, multiparity, lifestyle risk factors like smoking have been found to be associated with GBC. However, the strength of these associations remaining variable in different studies and all are not modifiable.

The pathogenesis of GBC remains to be understood. The presence of gallstones in majority of patients with GBC raises questions whether the calculi are merely associated or do they have a role in the pathogenesis of GBC. Both, the adenoma-carcinoma pathway, as well as the inflammation driven dysplasia-carcinoma pathway, has been proposed. However, there is lack of clarity as to which pathway is involved in the pathogenesis of GBC [2].

Numerous studies have been done to study the molecular alterations which lead to increased susceptibility to GBC. Molecular studies have failed to find clinically relevant biomarkers which would help in the early detection and treatment of GBC [3].

Lack of a recognizable premalignant state precludes screening. Studies for early diagnosis in high risk populations are necessary. The role of prophylactic cholecystectomy in high risk individuals is debatable. Prospective cohorts need to be identified in these high risk populations to determine the natural history of disease and development of cancer.

There is, at times, a failure to detect early gallbladder cancer. Number of patients have GBC incidentally detected at the time of cholecystectomy for gallstone disease, or at the time of histopathological examination of the gallbladder specimen [4]. Similarly, despite looking operable on conventional imaging, many patients of GBC have metastatic disease on laparotomy/diagnostic laparoscopy. Improved imaging techniques and use of functional imaging may help in both these circumstances.

The extent of surgery varies by centre and surgeon. Data suggests that a large number of patients are still treated with cholecystectomy alone and not by the full procedure. The extent of lymphadenectomy is still debatable as so is the role of extended lymphadenectomy. Only well designed trials can help define the optimal extent of lymphadenectomy.

Over the past few decades, the role of neoadjuvant treatment for most gastrointestinal cancers has evolved. Most of these cancers are now treated with preoperative chemotherapy/chemoradiation in order to make surgery less extensive along with increased overall survival. However, there has not been much positive clinical data generated for this strategy for GBC and at present, neoadjuvant treatment protocols are restricted to clinical trials only. Similarly, most of data for adjuvant treatment comes from studies which pool

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in GBC with other extrahepatic biliary cancers, which is a very heterogeneous subgroup, both clinically and biologically. There is lack of high quality data for the use of adjuvant treatment. Though chemotherapy is more commonly used as an adjuvant treatment, the role of radiation in the treatment of GBC remains to be defined and standardized.

Despite rapid developments in targeted therapies, the results of established molecules in the management of GBC have been disappointing. There is need for development of newer targeted agents keeping GBC in mind.

It is high time we realize that the evidence for treatment of GBC will have to come for the Indian subcontinent and not from the west. For conducting high quality studies, which will pave the way for standardizing treatment of GBC, it is imperative to form consortiums and research networks which will help pool patient data from across all high volume centers across India and conduct multicentre trials. The success of large collaborative groups of North America and Europe should be used as models for forming our own cooperative networks.

Gallbladder cancer provides an opportunity for Indian oncologists to stamp their contribution in cancer research and

treatment. Close coordination between clinicians and researchers and the formation of dedicated consortiums is the way forward. We should not look up to our colleagues in the Western hemispheres to provide us solutions for our problems. An Indian problem can be tackled best by an Indian solution.

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