

## Editorial-II

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### Diet and Gallbladder Cancer

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Carcinoma of the gallbladder (GB) is a common neoplasm in India. Its incidence varies from 27/100,000 in Chile to 1/100,000 in US.<sup>1</sup> The incidence in India ranges from 10/100,000 in Delhi to 2-3/100,000 in south.<sup>1</sup> The incidence is reported to be higher from the Gangetic belt however, due to absence of cancer registries in these parts the exact incidence cannot be commented upon. In Varanasi, it is estimated to be around 4.4% of all cancers and about 16% of all gastrointestinal cancers.

What causes GB cancer has always remained a matter of debate? A number of factors have been proposed though none of them are able to explain the GB carcinogenesis *in toto*. Cholelithiasis with or without chronic cholecystitis has been the forerunner among these causes.<sup>1</sup> Other factors that have been proposed are chronic infections like typhoid carrier state or Helicobacter infections, xanthogranulomatous cholecystitis, lipid peroxidation, genetic susceptibility etc. The list is never ending. The most attractive hypothesis that may explain the geographical variation is diet and life style factors. In this issue the study from Delhi population control study shed some more light on the issue. It was Fraumani in 1975, Who first tried to explain the epidemiology of biliary tract cancers and proposed that lithogenic factors like diet, pregnancies, hyperlipoproteinemia and familial tendencies may be responsible for carcinogenesis.<sup>2</sup> One must remember that it was a time when GB cancer was not separately registered as cancer by cancer registries around the world and was clubbed with other extrahepatic biliary tract cancers like cholangiocarcinoma. Kato et al in 1983, reported on 109 cases of GB cancer and 386 age and sex matched control, in what was probably the first case control study on this aspect.<sup>3</sup> They found an increased risk in patients with taste for oily food and intake of animal proteins and fats such as fish, eggs, meat, etc., ingestion of vegetables and fruits were low risk

factors for GB cancer.<sup>3</sup> A Polish case control study in 1992 showed increase risk with increase in total calorie intake, and a weaker association with carbohydrate, protein and cholesterol. An inverse relationship was observed with fibre intake, vitamin C and E. In 1995, Moerman et al showed a low risk associated with vegetable consumption and a higher risk of added sugar in desserts and drink to be associated with biliary tract cancer<sup>4</sup> and later showed the effects of life style factor. The same year in a multicentric study the body mass index, history of typhoid and family history of gallstones along with diet were found to be associated with gallbladder cancer. A case control study from SEARCH program of International Agency for Research on Cancer (IARC) reported elevated body mass index, high total energy intake, high carbohydrate intake (after adjustment for total energy intake), and chronic diarrhea to be associated with GB cancer.<sup>5</sup>

The 21<sup>st</sup> century saw an increased attention being paid to the diet and a number of studies were published including those from India. Our group was the first one to come up with an association of diet with GB cancer.<sup>6</sup> We demonstrated a significant reduction in odds ratio with the consumption of radish (OR 0.4; 95% CI 0.17-0.94), green chili (OR 0.45; 95% CI 0.21-0.94) and sweet potato (OR 0.33; 95% CI 0.13-0.83) among vegetables, and mango (OR 0.4; 95% CI 0.16-0.99), orange (OR; 0.45; 95% CI 0.22-0.93), melon (OR 0.3; 95% CI 0.14-0.64) and papaya (OR 0.44; 95% 0.2-0.64) among fruits.<sup>6</sup> On the other hand, a statistically insignificant increase in the odds was observed with consumption of capsicum, beef, tea, red chili and mutton.<sup>6</sup> Others too in the same year (2002) showed that the consumption of red chili and low intake of fruits and sugar to be associated with GB cancer

substantiating some of our results. A study from Pakistan too showed higher incidence with low consumption of fiber, vitamins and higher consumption of fat. They also found an increase in incidence in patients with prolong fasting which has not been demonstrated earlier. This progress was first reviewed by us in 2003 and later by others. In 2004 another study showed higher energy intake as possible cause of GB cancer. The results of other Indian studies were almost similar to what has been earlier reported that higher fruit and vegetable consumptions were associated with low risk of GB cancer.<sup>7</sup> They also found a low BMI for patients with GB cancer and attributed it to malnourishment and cancer cachexia associated with the disease. Obesity and poor socioeconomic condition has also been proposed as a risk factor for GB cancer but these could be surrogate for diet and nutrition.<sup>8</sup> Of the recent studies, tea drinking has been found to reduce risk, while body mass index, smoking and consumption of alcohol increase the risk.<sup>9,10</sup> A recent meta analysis evaluating the role of obesity and risk of GB cancer reporting on 8 cohort and 3 case control studies has shown higher relative risk of GB cancer in those who are over weight or obese, with this association to be stronger among women than men<sup>11</sup> In this issue of IJMPO, the study from Delhi Population based Cancer Registry reinforce the role of life style factors like tobacco and alcohol, past history of typhoid fever and cholelithiasis in GB carcinogenesis.<sup>12</sup> This is the first population based data from India.

Presently there is enough data to indicate that diet may play a role in GB carcinogenesis, however inherent problems with the study designs, high heterogeneity among studies and complexity of confounding variables cast a shadow of doubt. What is clear from the studies published so far is that a higher consumption of fruits, vegetable and fiber and low consumption of meat, fat, and calories may prevent development of GB cancer. The need for further well designed, large, multicentric cohort and case control studies cannot be understated.

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