Cancer Risk and Diet in India

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Abstract:

India is a developing country with one of the most diverse populations and diets in the world. Cancer rates in India are lower than those seen in Western countries, but are rising with increasing migration of rural population to the cities, increase in life expectancy and changes in lifestyles. In India, rates for oral and oesophageal cancers are some of the highest in the world. In contrast, the rates for colorectal, prostate, and lung cancers are one of the lowest. Studies of Indian immigrants in Western societies indicate that rates of cancer and other chronic diseases, such as coronary heart disease and diabetes, increase dramatically after a generation in the adopted country. Change of diet is among the factors that may be responsible for the changing disease rates. Diet in India encompasses diversity unknown to most other countries, with many dietary patterns emanating from cultural and religious teachings that have existed for thousands of years. Very little is known, however, about the role of the Indian diet in causation of cancer or its role, if any, in prevention of cancer, although more attention is being focused on certain aspects of the Indian diet, such as vegetarianism, spices, and food additives. Of particular interest for cancer prevention is the role of turmeric (curcumin), an ingredient in common Indian curry spice. Researchers also have investigated cumin, chilies, kalakhar, Amrita Bindu, and various plant seeds for their apparent cancer preventive properties. Few prospective studies, however, have been conducted to investigate the role of Indian diet and its various components in prevention of cancer. From a public health perspective, there is an increasing need to develop cancer prevention programs responsive to the unique diets and cultural practices of the people of India.

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The relationship between diet and health has been recognized throughout recorded history. Disease prevention through healthy preparation of foods and eating habits has been discussed in religious and civil writings for thousands of years.[1] Since the 19th century, western scientific methodologies have been applied to the study of diet and disease with the intent of reducing the disease burden from non-communicable diseases (NCD) such as cancer, coronary heart disease (CHD), and other conditions endemic to societies after the advent of industrialization. Ecologic, observational, and laboratory studies generally agree that eating a diet high in vegetables, fruits, and other plant-based foods; low in animal fats and low in salt content, along with maintaining a healthy weight, not using tobacco in any form, and being physically active can reduce the risk of cancer, CHD, and other chronic diseases.[2,3] Diet-related NCDs are of great concern to researchers assessing the impact of changes in diet in "developing" countries, such as India. Trends, based on current and projected data, in nutritional and disease status indicate that these countries face considerable challenges as under-nutrition evolves into over-nutrition as the community becomes "developed"."[4]

Trends in nutritional and disease status indicate that "developing" countries face considerable challenges as under-nutrition evolves into over-nutrition as the community becomes "developed".

India, a country in transition from a "developing" to a "developed" nation, is home to more than one billion people, with an ever-increasing middle class population with greater disposable incomes. Fourteen major languages and hundreds of dialects are spoken.[1] Dietary customs and habits in India are diverse, owing in part, to the range of religions in the society, many of which provide specific dietary guidance for their followers. Furthermore, there is a tradition of linking vegetarianism with medicine. For example, Ayurveda provides dietary guidance and proscriptions that have been developed over millennia to prevent and treat multiple ailments, including CHD, cancer, and diabetes. Cancer rates in India are rising as development

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progresses, with a changing profile of burden at different cancer sites. According to the World Health Organization (WHO), cancer rates in India are considerably lower than those in more developed countries such as the United States (see Table 1).[5] Data from population based cancer registries in India show that the most frequently reported cancer sites in males are lung, oesophagus,. stomach, and larynx. In females, cancers of the cervix, breast, ovary, and oesophagus are the most commonly encountered.[6]

Contrary to what is seen in most developing countries, India has some of the highest CHD rates in the world,[1] with urban rates being three times higher than rural rates.[7] In addition, rates for obesity and diabetes are increasing dramatically in urban areas and in high-income rural residents.[4,7] For example, the prevalence of diabetes in urban areas has been reported at 9-16%, more than four times the prevalence of two decades ago.[8] Diet appears to be related to the high rates of CHD, obesity, and diabetes, although a genetic component may exist in some cases. In recent decades, consumption of foodgrains also has shifted from coarse grains (e.g., barley, rye, maize, millet, and sorghum) to refined rice and wheat.[4]

Studies of immigrants provide insight into the contributions of environmental, behavioural, genetic, and lifestyle factors that determine risks for chronic diseases in Indians. Various immigration studies have included Asian Indians. Trends for cervical cancer incidence were investigated in a population-based study using 1968-1987 data from the Singapore Cancer Registry.[9] Incidence rates were highest in women from India, followed by China and Malay. Data from 1968-1982 remained the same when compared in 5-year periods, although rates declined in each group.[9] Data from the National Cancer Registry of Malaysia from 1987-1989 showed that site-specific cancers differ among Malays (larynx and oesophagus), Chinese (nasopharyngeal), and Indians (mouth cancers), and that Malaysia is in a cancer-transitional state from less industrialised (frequent sites: stomach, cervix, lung) to industrialised (frequent sites: lung, breast, rectum).[10]

The Singapore Cardiovascular Cohort Study (SCCS) and the National University of Singapore Heart Study (NUSHS) investigated the relationship of risk factors for CHD and related conditions in Chinese and Indian immigrant populations and in indigenous Malays residing in the state. The NUSHS assessed dietary factors to determine the impact of diet on increasing rates of CHD, cerebrovascular disease, and cancer, and found vitamin C levels were lower in Malays and Asian Indians, which may have been responsible for higher CHD and cancer rates in those groups.[11] The authors suggest that a low intake of fresh fruits and high cooking temperatures in Malay and Asian Indian dishes may account for the low levels of vitamin C. Recent case-control studies in Asian Indian immigrants in the United Kingdom and the United States identified high levels of homocysteine as a risk factor for the development of CHD[12,13] and cancer.[14]

Rates of certain cancers are changing in India with ongoing economic development, increase in life expectancy and rise in adoption of a Western lifestyle.

Table 1: Comparison of cancer rates in India and the United States[5]

	India		United States	
	Male	Female	Male	Female
Cancer Rates, all sites except skin	99.0	104.4	361.4	283.2
Oral	12.8	7.5	6.3	3.7
Oesophagus	7.6	5.1	4.9	1.4
Stomach	5.7	2.8	7.3	3.6
Lung	9.0	2.0	58.6	34.0
Colon/Rectum	4.7	3.2	40.6	30.7
Breast	—	19.1	—	91.4
Ovary	—	4.9	—	10.6
Cervix	—	30.7	—	7.8
Endometrial	—	1.7	—	15.5
Prostate	4.6	—	104.3	—
Liver	2.3	2.0	4.2	1.7
Bladder	3.2	0.7	23.4	5.4
Kidney	1.2	0.5	11.2	6.0
Melanoma of the skin	0.3	0.2	4.2	1.7

Rates are per 100,000 population

Dietary Factors And Lifestyle

India's rapid urbanization is characteristic of a country changing status from a "developing" to a "developed" country. Dietary changes, reductions in physical activity, and increasing obesity generally follow this transition, especially as urbanization occurs. Diet in India has been associated with the risk of chronic disease, although few of these associations have been investigated into or quantified adequately. Though not a comprehensive review, the following sections discuss factors of diet and lifestyle that may contribute to the growing burden of chronic diseases in India (summarized in Table 2).

Obesity and Physical Activity

Obesity and lack of physical activity are associated with increased risk at various cancer sites, including breast and endometrial cancer.[2] In India, increases in the rates of obesity, central adiposity, and waist-hip ratio associated with urbanization are seen in every region and are highest among those with the highest levels of education[18] and income.[7] Energy balance, which includes maintaining ideal weight through physical exercise, has been associated with decreased risk of

Table 2: Comparison of risk factors for cancer in India and the United States[15-17]

	India	United States
Physical Activity	Not Available	23.5%§
Obesity*	M: 3%	M: 20%
	F: 14%	F: 23%
Energy Intake†	M: 1812±645	M: 2,517
	F: 1395±379	F: 1,764
Dietary Fat Intake‡	24-27%	30%
Carbohydrate Intake‡	60%	50%
Protein Intake‡	13%	15%

*Obesity defined as BMI ≥30 kg/m^2, †Energy intakes per day in kilocalories ‡Percentage of calories per day, §Prevalence of regular, sustained physical activity ≥5 times per week and ≥30 minutes per occasion

breast cancer.[2] There are few large cross-sectional studies of energy balance in India.[19] Among urban populations, energy intake has increased at the same time that energy expenditures have decreased, due in part to employment in industries reliant on mechanization.[2] No comprehensive study of physical activity in India has been done, but small studies of selected populations suggest that levels of physical activity are inadequate to meet recommendations for prevention of chronic diseases.[20,21]

Vegetarian diets

A large percentage of Indians, particularly Hindus, practice vegetarianism and avoid meat and fish products in their diet. Vegetarian diets have been associated with decreased risk for prostate cancer.[22] Case-control studies that compared non-vegetarian and vegetarian diets and alcohol and tobacco use in India have reported that vegetarians have a reduced risk of oral,[23] oesophageal,[24] and breast cancers.[24] Vegetarian diets rely on pulses (e.g., beans, chickpeas, and lentils) as a source of protein, and pulses have been significantly associated with reductions in cancer.[25,26]

Diet in India is a promising field for researchers interested in cancer prevention because very few large-scale, well-designed studies have been conducted.

Dietary Fats and Fiber

Diets high in saturated fats have been associated with increased risk for cancer.[2] Fat intake, especially saturated fat, is increasing in the middle class in India, although some rural residents traditionally have had a high intake of ghee (clarified butter, high content of saturated fat), as well.[27] Studies have given equivocal results regarding the link between fat intake and the risk of cancer.[2,28] Large epidemiological studies have identified a possible association between increased dietary fibre and a decreased risk for cancers of the colon and breast.[2] No large studies on dietary fibre have been conducted in India, and rates of colon and breast cancer are low compared to those in western societies. The Indian diet, which generally includes adequate levels of vegetables, fruits, and fiber-rich grains, may provide some protection against increased risk for these cancers.[2]

Spices and Food Additives

Diet in India developed over thousands of years and is based on a mix of religious and secular beliefs. For example, Ayurveda medicine prescribes more than 700 plant-based medicines that contain spices and food additives to encourage good health. Many of these foodstuffs have been studied for their disease prevention capabilities, including turmeric (curcumin), cumin, chilies, kalakhar, Amrita Bindu, and various plant seeds. Among the most studied in recent years is turmeric, an ingredient in the common Indian curry and a spice that has been shown to be a potent antioxidant and anti-inflammatory agent with additional promise as a chemo-preventive agent. In a study in human blood cancer cell lines, turmeric suppressed and destroyed blood cancer cells.[29] Turmeric has been shown to suppress tumour initiation, promotion, and metastasis in experimental studies.[29] To illustrate, turmeric may block the activity of nuclear factor kappa-B (NfκB), which, in an activated state, appears to be associated with cancer cell growth in many cell types.[29] Turmeric also has been found to inhibit the growth of 19 clinical strains of *Helicobacter pylori*, a carcinogenic bacterium linked to the increased risk of adenocarcinoma of the stomach and colorectal adenomas.[30]

Amrita Bindu, a dietary supplement that is a salt-spice-herbal mixture, was found to protect rats against cancer induced by *N*-methyl-*N*-nitrosoguanidine, a potent carcinogenic nitrosamine.[31] Possible mechanisms that explain the chemo-preventive role of Amrita Bindu include prevention of depletion of vitamins A, C, and E and of the anti-oxidant enzymes glutathione peroxidase and superoxide dismutase in the liver of rats. These actions in turn, prevent the rise of lipid peroxidation in the plasma and liver; and enhance glutathionine actions in both blood and liver.[31]

A recent study investigated the anti-carcinogenic effects of nine Indian spices on induction by dietary benzo[a] pyrene (B[a]P) of squamous cell carcinomas (SCC) of the stomach in mice and induction by dietary 3'-methyl-4-dimethylaminoazobenzene of hepatomas in rats.[32] Cumin seeds and basil leaves significantly decreased the incidence of both SCC and hepatomas; poppy seeds significantly inhibited B[a]P-induced SCC; and the other six spices showed no effect.[32]

Studies on spices and food additives have been conducted *in vitro* and in animal studies. Because of intriguing findings from these studies, there is a need to investigate these dietary factors in human studies.

Micronutrients

Micronutrients play a significant role in maintaining health and preventing disease, including cancer, through a wide range of mechanisms: anti-oxidation, anti-proliferation, and repair of DNA damage.[2] Direct and indirect relationships between micronutrients and health have been described in experimental, epidemiological and clinical trials.[2] Vitamin deficiencies, specifically of vitamins A, C and E, may contribute to the high prevalence of oral cancers in India.[33] A study carried out in rural India found that the presence of lesions was associated in patients with oral pre-cancerous lesions with low plasma levels of vitamins E and β-carotene.[34] A study of Kurchias (a tribal population in Kerala, India, who consume a diet high in micronutrients and have a low prevalence of CHD and other chronic diseases of aging, including cancer) found that levels of serum vitamins A and E were inversely related to levels of lipid peroxides and CHD risk factors.[35] Micronutrient deficiencies of iodine, iron, and vitamin A are highly prevalent in Indian children. Among 6-14-year-olds, goiter, caused by iodine deficiency and related to thyroid cancer, has a prevalence rate of 0.33 to 2.4%.[36]

For cancer prevention, the National Institute of Nutrition recommends a diet that includes high intake of fresh vegetables and fruits, with spices such as turmeric, in adequate amounts.

Dietary Guidance in India

For the past 70 years, the Indian Council of Medical Research (ICMR) has produced information on nutritional requirements specific to the population of India. Approximately every 10 years, the ICMR updates nutrition recommendations based on evolving information from surveys conducted by the National Institute of Nutrition (NIN), Hyberabad.[37] The latest survey, completed in 2000, found that the Indian diet and nutrient intakes have hardly changed in the last 20 years. For cancer prevention, the NIN recommends a diet that includes high intake of fresh vegetables and fruits, with spices such as turmeric, in adequate amounts.[38]

Cancer sites

Oral Cancers

Incidence rates for oral cancer in India are among the highest in the world;[5] most are associated with diet, weight, and other lifestyle factors.[33] A significant lifestyle risk factor is betel quid (paan) chewing, a practice that is highly prevalent in India. Betel quid contains a variety of ingredients such as lime, catechu, and areca nut and is often mixed with tobacco. A case-control study in Southern India investigated the influence of paan, body mass index (BMI), diet, infections, and sexual practices on oral cancer.[39] BMI was inversely associated with oral cancer, and paan chewers with low BMI had a very high risk of developing oral cancer. Frequent consumption of fish, eggs, a variety of raw and cooked vegetables, and fruit was associated with a decreased risk of oral cancer.[39] A study on reverse smoking (i.e. smoking with the glowing end inside the mouth) revealed that use of tobacco in this form conferred a 5.19 times higher risk of oral pre-cancerous lesions of the palate than did use of chewing tobacco.[40] Diets low in vegetables and fruits and high in alcohol increase the risk of oral cancers.[2]

Oesophageal Cancer

In India, the incidence of oesophageal cancer is moderately high and is associated with certain diets and lifestyles. Oesophageal cancer is the second most common cancer among males and the fourth most common cancer among females according to combined data from cancer registries in India.[6] Among risk factors for oesophageal cancer in India, betel quid chewing carries a relative risk of 1.5 to 3.5. Salted tea, made by adding sodium bicarbonate, has shown high methylation activity and can result in endogenous formation of nitrosamines.[41] Commonly used fresh and sun-dried vegetables and chilies also have a high content of nitrates or nitrosamines and may be associated with higher rates of oesophageal cancer. Various foods and food additives have been studied for their association with this disease.[42] For example, kalakhar is a highly alkaline substance made from the charred false stem or from the skin of a particular variety of banana that is used as a coffee decoction or during the preparation of curry or "dal." Daily use of kalakhar greatly increased the risk (OR=8.0) of oesophageal cancer.[42] In the same study, spicy foods (OR=5.1) and chilies (OR=6.9) also resulted in a significantly increased risk. Another case-control study found alcohol (OR=7.81 with daily use), chewing betel leaf with tobacco (OR=3.16), bidi smoking (OR=1.95), and a diet low in vegetable consumption (OR=1.88) to be risk factors for oesophageal cancer.[43]

Endometrial, Cervical, and Ovarian Cancers

Cancer of the female reproductive tract has a high incidence amongst Indian women. Human papilloma virus (HPV) is the most prevalent risk factor for cervical cancer and has been

associated with cancer of the ovaries and endometrium.[44] Environmental and dietary risk factors for cervical, ovarian, and endometrial cancers have been investigated in case-control and cohort studies.[2] Cervical cancer is the most common cancer of the female genital tract in India, with approximately 100,000 new cases occurring each year. This accounts for almost 20% of all new cases diagnosed in the world annually.[45] The incidence higher in rural areas, where prevention and screening programs are not as easily available as in urban areas.[46,47] A review of studies on diet and cancers of the cervix,[48] ovary[49], and endometrium[49] have provided equivocal results. Some of the studies have suggested that a diet high in carotenoids, vegetables, and fruits may reduce the risk of cervical, ovarian, and endometrial cancers; high intake of vitamins C and E may reduce the risk of cervical cancer; and a diet high in fish may reduce the risk of ovarian cancer.[2]

Breast Cancer

In India, the incidence of breast cancer is increasing, with an estimated 80,000 new cases diagnosed annually. The incidence of breast cancer increased by approximately 50% between 1965 and 1985.[50] Much of this increase may be associated with greater urbanization and improved life expectancy. The incidence rates, education level, and income are higher in urban areas compared with rural areas.[51] In addition, age at puberty and pregnancy-related factors, such as parity, age at giving birth to the first baby, and number of children, are factors possibly related to breast cancer. Few studies of diet and breast cancer in India have been published. The nutrition guidelines follow the World Cancer Research Fund recommendations that advocate having a diet containing vegetables and fruits in large amounts, reducing the intake of saturated fats, and increasing physical activity.[2]

Lack of well-designed, prospective epidemiological studies necessitates additional research to assess the impact of diverse dietary habits, religious practices, and lifestyles on prevention of cancer in India.

Stomach Cancer

Compared to other countries, stomach cancer incidence rates are moderate to low in India, although certain populations, such as those in the Chennai area, have very high rates.[6] A recent case-control study in Mumbai found that consumption of dried fish (OR=12.4) increased the risk while green tea consumption (OR=0.4) decreased the risk of having stomach cancer.[52] A prospective case-control study from Trivandrum evaluated dietary risk factors for stomach cancer and found that high consumption of rice (OR=3.9), spicy food (OR=2.3), chili (OR=7.4), and high-temperature food (OR=7.0) increased the risk of developing stomach cancer.[53] Fried foods are associated with higher rates of cancer due in part to the production of carcinogenic or mutagenic heterocyclic amines (HA) during the cooking process.[2] Case-control and prospective studies have reported an increased risk of stomach (RR=2.5),[54] colon (OR=2.7),[55] and bladder (RR=2.6)[56] cancers with moderate to heavy consumption of fried foods. Studies of mice fed with deep-fried vegetables and salted or sun-dried Ribbonfish, which is commonplace in Indian cooking, reported a 20 percent increase in gastric carcinoma.[57] The rise has been attributed to the presence of polycyclic aromatic hydrocarbons produced by the cooking method.[57] As mentioned earlier, the use of the spice turmeric is associated with a reduced risk of stomach cancer, in part because of its protective effect against the carcinogenic bacterium *H. pylori*, a major risk factor for stomach cancer.[33]

Summary

Diet is an important factor in cancer aetiology and prevention in India. As a society, Indians have one of the most interesting diets, with many unique dietary constituents that have promise for cancer prevention. Very few well-designed, prospective epidemiological research studies exploring the relationships between diet and lifestyle and cancer have been carried out in India (see Table 3).

Table 3: Possible Dietary and Other Factors Associated With Cancer in India*

	Decreased Risk	Increased Risk
Oral cancer	Diet high in vegetables and fruits,[39] Fish[39] Eggs[39]	Betel quid chewing[38] Reverse smoking (palate)[40]
Esophageal cancer	Diet high in vegetables[43]	Betel quid chewing[43] Chillies[41] Salted tea[41] Kalakhar[42]
Endometrial cancer	Diet high in vegetables and fruits[2] Diet high in carotenoids[2]	High body mass index[2] Saturated fat intake[2] Human papillomavirus (?)[44]
Cervical cancer	Vitamins C and E[2]	Human papillomavirus[44] Tobacco use[2]
Ovarian cancer	Diet high in fish[2]	Saturated fat intake(?)[2] Human papillomavirus (?)[44]
Breast cancer	Diet high in vegetables and fruits[38] High physical activity (possible)[2]	Diet high in saturated fats[2] High body mass index[38] Saturated fat (?)[2]
Stomach cancer	Green tea,[52] Turmeric[30] Cumin,[30] Basil,[30] Tapioca[53]	Dried fish[52] High-temperature foods[53] Chillies[53] Spicy foods[53] High consumption of rice[53] *Helicobacter pylori*[30]

*Because there have been few large prospective epidemiologic studies in India on many of the factors listed in this table, the information given has been drawn from the best available evidence.

Additional research is needed to assess the impact of diverse dietary habits, religious practices, and lifestyles on prevention of cancer. Cancer detection and prevention efforts can have enormous benefits for developing countries by reducing future disease burden while saving economic resources for needed improvements in societal infrastructure. As development and mechanization continue into the 21st century, India must grapple with a transition from the burden of communicable diseases to the burden of NCDs.

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