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REVIEW ARTICLE

Head and neck cancer in India – review of practices for prevention policy

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India, with a population of over a billion is likely to increase global concern on cancer, particularly that of head and neck. The increasing immigration of Indians is likely to influence other parts of the world and an analysis of cancer-related practices could serve as a model for defining cancer-prevention strategies across the globe. The objective of this study was to review the anti- and pro-carcinogenic practices in India pertaining to head and neck cancer. The published literature on practices, compounds/chemicals/crude reparations related to the head and neck cancer in India was retrieved for analysis, while unauthentic or local information was discarded. The anti-carcinogenic practices prevalent in India consisted of classically varied diet being predominantly vegetarian, along with spices, condiments, beverages etc. The pro-carcinogenic practices predominantly include all shades of alcoholism and tobacco intake. Moreover, the diverse culture of the country reflects unique regional practices. The enormous diversity in practices related to head and neck cancer in India is very unique and interesting. Cancer prevention strategies need to focus on these trends to define a better global prevention.

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Introduction and methods

India, the most densely populated country with over a billion population, is unique in its extreme diversity in climate and culture. The innumerable ethnic groups, religions and more than 18 different official languages across the country reflect its extreme diversity amidst all nations of the world. India is known for an extremely high incidence of head and neck cancer (especially oral and oropharyngeal) owing to the unique use of tobacco and its related products. However, such a varied diversity also includes other innumerable cancer-related practices that need to be analyzed and taken into consideration while planning a prevention strategy for resident and immigrant Indian population. World-wide published English literature (pub med) was searched for different combinations of words like 'cancer', 'practices' & 'India' with 'oral', 'oropharyn*', 'nasopharyn*', 'pharyn*', 'laryn*', 'nose', 'nasal', 'paranasal', 'sinus' 'ear', 'salivary gland', 'thyroid', 'post cricoid', 'temporal' or 'oesophag*'. A similar search for the relevant information was undertaken through 'yahoo' search engine and also obtained from the web sites of WHO (World Health Organization), IARC, UICC (International Union against Cancer), INCTR (International network for Cancer Research and Training) and ICMR (Indian Council of Medical Research). The regional prevalence was confirmed through a second level of data search by substituting the names of various states instead of 'India' in the above permutations and combinations.

Observations and results

The rapid urbanization of India, with its ongoing transition to a developed nation, reflects the dietary changes (Shetty, 2002), increasing obesity and reductions in physical activity. Diet in particular has been associated with the risk of many chronic diseases including cancer, although only a few of these associations have been investigated and quantified accordingly. Obesity and lack of physical activity (Tables 1 and 2) are associated with increased risk at various cancer sites (World Cancer Research Fund, American Institute for Cancer Research, 1997).

Vegetarian diet

Majority of Indians particularly Hindus are vegetarians and hence avoid meat except fish in certain areas. Also,

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Table 1 Percentage prevalence of obesity amongst Indians (BMI > 25 kg m^{-2})

Age groups	*Male*	*Female*
20–24	10.4	13.5
25–29	17.9	21.4
30–34	25.2	37.2
35–39	30.7	40.3
40–44	35.9	45.5
45–49	33.3	45.9
50–54	31.2	44.4
55–59	27.3	41.4
60–64	23.1	40.3
65–69	24.8	35.7
>70	16.2	29.1

Adapted from WHO Global NCD Infobase (Ramachandran *et al*, 2001).

Table 2 Percentage prevalence of physical inactivity amongst Indians

Age group	*Males*	*Females*
18–29	9.0	11.9
30–39	8.4	14.2
40–49	7.2	20.0
50–59	11.8	14.0
60–69	13.8	23.9
18–69	9.4	15.3

Early release weighted data from WHO World Health Survey. http://www.who.int/ncd_surveillance/infobase/web/InfoBaseCommon/Shared/mdDetails.aspx?surveyCode=101711a1.

there is a section of 'eggetarians' amongst the vegetarians who apart from milk consume only egg as a source of animal protein. On the other hand, Muslims are predominantly non-vegetarians, but the use of processed canned meat is much less prevalent in India than in the western world. Casimiro (2002) has shown that on one hand, the processed meat enhances cancer risk; on the other hand, fish consumption reduces the cancer risk. A reduced risk for head and neck cancer amongst vegetarians has been reported (Rao *et al*, 1994; Rao, 2003). The vegetarian diets rely on pulses (e.g. beans, chickpeas, *dal*) as a source of protein, and these pulses have been significantly associated with a reduced risk of cancer (Jain *et al*, 1999). Vegetarian diet is also a rich source of bioactive phytochemicals or bionutrients, which have an important role in cancer prevention (Rao, 2003). The major classes of phytochemicals with disease preventing function are dietary fibers, antioxidants, detoxifying agents, immunity potentiating agents. Foods rich in these chemicals and exhibiting disease-protecting potential are called functional foods. Indian habitual diets that are based predominantly on plant foods like cereals, pulses, oils and spices are all good sources of these classes of phytochemicals particularly dietary fibers, vitamin E, carotenoids and phenolic compounds. Krishnaswamy and Polasa (1995) too have stressed on the dietary intervention for cancer prevention by recommending plentiful consumption of fresh fruits and vegetables. As India's economy is predominantly based on agriculture, the majority of Indian population has access and prefers fresh vegetables to deep frozen and processed vegetables as seen in the western world. The widely used cruciferous vegetables (cabbage, cauliflower, etc.) across the country are known to play an important role against the risk of cancer due to the presence of glucosinolates (Talalay and Fahey, 2001). On the other hand, although the staple consumption of phytoestrogen-rich food has been correlated with reduced incidence of breast cancer (Limer and Speirs, 2004), its implication for head and neck cancer has not been well established except that it may have some chemopreventive role in hormone-dependent cancers.

Grapes and groundnuts (peanuts) are grown in abundance across the country and are known to contain resveratrol, a natural food micro-component with potent anticancer (chemopreventive) properties. A processed, packaged, ready-to-eat food item called 'dalmoth' that includes peanuts pulses and cereals is an extremely popular snack across the country. This is analogous to packaged potato chips but with much more nutritive value. On the contrary, Takezaki *et al* (2001) found that consumption of carrot, pumpkin, egg and coffee was associated with increased odds ratio for squamous cell carcinoma in males.

The use of tea is widely prevalent in India. It is well established that the antioxidant properties of tea polyphenols (catechins) afford protection against various types of cancer. Both green tea and black tea have been shown to have an equal potential in modulating arsenic-induced genotoxicity (Sinha *et al*, 2005). Tea has been the most common beverage used across the country for several decades. The addition of honey and *tulsi* (*Osimum sanctum*) as often used in India enhances its anticancer potential along with its desensitizing (to allergens) role. It is also very common to see *ginger-tea* as a substitute of *tulsi-tea* in India. However, Hiranandani (1975) considered the slaked lime present in the Indian tea mixture as causing irritation leading to leucoplakia and post cricoid carcinoma. Stocks (1970) has correlated tea drinking with laryngeal cancer in women.

The use of fresh lemons to enhance the palatable quality of food is a very common practice. Surjyo and Anisur (2004) have demonstrated the protective action of L-ascorbic acid, active ingredient of lemon, as an antioxidant against cancer. It is a common practice in India to prepare pickle or *achaar* from the whole lemon including its peel. Perillyl alcohol, a monoterpene and an analog of d-limonene, is found in the citrus peel and has been shown to be an important anticancer (chemopreventive) agent (Einspahr *et al*, 2003). Esteve *et al* (1996) found that the people with the highest level of vitamin C intake were at low risk for laryngeal cancer compared with people in the lowest quintile.

Dietary fat and fibers

Diets high in saturated fats have been associated with increased risk for cancer (World Cancer Research Fund, American Institute for Cancer Research, 1997). Fat (particularly saturated) intake is increasing in the

middle-class section in India. In most of the rural areas, the traditional intake of *ghee* (high content of saturated fat, derived from butter) is also frequently practiced (Ghafoorunissa 1998). Law (2000) has shown equivocal results regarding the link between fat intake and cancer risk. The particular anticancer role of the roughage component of the fiber content of Indian diet is well established for colon cancer, but no report is yet available for its impact on head and neck cancer. In general, the Indian diet that predominantly includes vegetables, fruits and fiber-rich grain may provide some protection against increased risk for cancers.

Spices and food additives

Indian diet has evolved over thousands of years as a result of secular and religious beliefs. Worth noting is the Ayurvedic medicine that prescribes more than 700 plant-based medicines containing spices and food additives to encourage good health. Several of these foodstuffs such as turmeric (curcumin), cumin, chilies, *kalakhar*, *Amrita Bindu* and various plant seed have been studied for their anticancer potential. The most extensively studied in the recent years is the turmeric (rhizome of the plant *Curcuma longa*), an ingredient of the common Indian curry and a spice that is supposedly a potent antioxidant and anti-inflammatory agent with an additional potential of being chemoprotective. Aggarwal *et al* (2003) have done an outstanding work on curcumin and have shown it to block the activity of nuclear factor κB, along with establishing its role in suppressing tumor initiation, promotion and metastasis. Its multiple actions on STAT3 and IL-8 have also been noted making it a very potential agent for cancer chemoprevention. Curcumin and genisten are two natural products of plants obtained from turmeric and soybeans, which are able to antagonize the carcinogenic potential of pesticides endosulphane and DDT on estrogen-positive breast cancer. As it is difficult to remove pesticides completely from the environment or the diet and as both turmeric and soybeans are not toxic to humans, their inclusion in diet to prevent hormone-related cancers deserves consideration. Another flavinoid antioxidant, silymarin, isolated from milk thistle, exerts exceptionally high to complete anti-carcinogenic effects in tumorigenesis model of epithelial origin (Zi *et al*, 1998). Ginger, a well known vegetative product used in Indian diet, is the rhizome of *Zingiber afficinale* (Roscoe Zingiberaceae) and has been found to prevent growth of colorectal cancer cells by virtue of its ingredient gingerol.

Amrita Bindu is a salt-spice-herbal mixture used as a dietary supplement in India and has been found to protect rats against cancer induced by *N*-methyl-*N*-nitrosoguanidine, a potent carcinogenic nitrosamine (Shanmugasundaram *et al*, 1994). The possible mechanisms that explain the chemo preventive role of Amrita Bindu include prevention of depletion of vitamins A, C and E and of antioxidant enzymes glutathione peroxidase and superoxide dismutase in the liver. These, in turn, prevent the rise of lipid peroxidation in the plasma and liver and enhance glutathione actions in both blood and liver. Aruna and Sivaramakrishnan (1992) investigated the anti-cancer effects of Indian spices and found the curcumin, poppy seeds and basil leaves to decrease significantly the incidence of squamous cell cancer in mice.

A very important association of Indian population, both in terms of dietary supplement and in terms of religious attachment, is a herb *tulsi* (*O. sanctum*). This herb (leaves) has proven adaptogenic properties. Prashar *et al* (1994) have concluded a chemopreventive role of *O. sanctum* extract on cancer in mouse. On the other hand, the use of *pudina* (mint) or *Mentha piperita* as an addendum to Indian meals in the form of a palatable paste 'chutney' is quite prevalent. This has chemoprotective and radioprotective potentials by virtue of the presence of eugenol, caffeic acid, rosmarinic acid and alpha tocopherol that have been shown to have antioxidant and anti-peroxidant properties (Kumar *et al*, 2004).

Micronutrients

These play a significant role in maintaining health and preventing cancer through various mechanisms including antioxidation, antiproliferation and repair of DNA damage. Tandon *et al* (2000) have suggested the contribution of vitamin deficiencies (A, C and E) to the high prevalence of oral cancers in India. Similarly, low plasma levels of vitamin E and betacarotene, especially those seen in rural India, have been associated with oral precancerous lesion (Patel *et al*, 2001). Vitamin A (beta-carotene) has been shown to have an antioxidant effect that in turn may be cytoprotective against oxidative DNA damage (Bendich and Shapiro, 1988; Krinsky, 1991). Kapil *et al* (2003) reported a strong association of cancer larynx with vitamin A, vitamin C, and zinc, but they could not comment upon the cause–effect relationship. A high consumption of micronutrients amongst 'kurchias' tribe is associated with low prevalence of cancer. The role of iodine deficiency related to cancer of thyroid is well established and is in fact rampant in the sub-Himalayan zone. The role of vitamin D_3 as an effective antitumor drug has been reported (Karmakar *et al*, 2002). In a hot country like India, the natural climate with a plenty of sunlight acts a natural source of vitamin D. For reasons of tanning of the skin and presence of plenty of melanocytes, Indians are less prone to sunburn-related diseases.

Tobacco and associated products

A World Health Organization (1999) report stated that 10% of all smoking-related deaths and loss of productivity in the world are estimated to come from India. It is noteworthy that head and neck cancer is supposed to be a major a part of this entire smoking-related morbidity/mortality and the current scenario is expected to still get worse in India. Following trends have been observed during analysis of data from the 52nd round of National Sample Survey (NSS), a national household survey conducted across India (Neufeld *et al*, 2005): men are reported to smoke tobacco more than chewing, while the reverse trend is seen in women; regular smoking has

been found to be greatest in fifth decade for men, while in eighth decade for women; and the greatest prevalence of tobacco chewing is seen in seventh decade amongst both genders. Several interesting observations were found: First, men were 26 times more likely than women to be regular smokers and four times more likely to chew tobacco. Secondly, schedule caste/tribe population was 1.4 times more likely to be regular smokers and 1.5 times more likely to be tobacco chewers compared with non-schedule caste/tribe population. Thirdly, population below poverty line showed greater relative odds of regular tobacco chewing, but not for smoking. Fourthly, the rural population (as compared to urban) was twice as likely to report tobacco chewing and 1.5 times as likely to report tobacco smoking. Finally, the uneducated class, as expected, was more likely to be a regular user of substance abuse (Tables 3 and 4).

The impact of tobacco chewing is well known and especially in India where the incidence is maximum across the world and that too in multiple forms. The harmful effects of tobacco have been well documented in India's history (Chattopadhayya, 1993). Indians (immigrants) have popularized the habit of betal chewing in the new world as well. Yoganathan (2002) reports the same for New Zealand and Australia, where areca nut preparations are widely available. The regular use of betal stains the mucosa, gums and teeth. This habit is discouraged in many countries for reasons of its oncogenic, addictive and dysesthetic properties, but it is very common for any public place in India (especially northern central) to have innumerable betal stains in virtually every nook and corner.

Table 3 Prevalence of tobacco use in India (1998–1999)

	Smoking (prevalence %)		*Smokeless tobacco (prevalence %)*	
Age group (years)	*Male*	*Female*	*Male*	*Female*
15–19	4.4	0.2	9.4	2.1
20–24	13.7	0.6	20.3	4.3
25–29	25.1	1.1	28.0	8.0
30–39	37.6	2.2	31.4	12.3
40–49	45.0	4.0	35.6	18.6
50–59	45.3	5.7	35.4	22.8
>60	38.2	5.3	37.6	25.0

Adapted from WHO Global NCD Infobase (2002).

Table 4 Prevalence of tobacco use in India (2003) in males: Definition: current user; Tobacco type: unspecified

Age group	*Males: prevalence (%)*
12–18	21.7
19–30	53.2
31–40	66.4
41–50	70.8
51–60	70.4
12–60	55.8

Adapted from WHO Global NCD Infobase (2002).

Parkin *et al* (1997) reported downward trends in male incidence of oral cancer in developing countries in contrast with the increasing lung cancer rates. Hence, they are supposedly not attributable to changes in cigarette smoking, but in tobacco chewing that has diminished in India threefold from 1951–1952 to 1980–1981 (Jayant and Yeole, 1987). Such decreasing trends in cancer rates have also been attributed to changing dietary habits in terms of increase in fruits, vegetables and protein intake (Martinez, 1969; La Vecchia *et al*, 1997). Franceschi *et al* (1999, 2000) stated that in non-smokers, substantial increases in oral cancer appear to be more closely related to changes in alcohol consumption. The optimistic data of decreasing trends in rates as reported by the foreign authors may not truly reflect the current status of increasing use of chewable tobacco with increased predisposition to oral cancer in the northern part of India, (Mehrotra *et al*, 2003). It is worth mentioning at this point that bidi smoking is more harmful than cigarette smoking (Rahman *et al*, 2005) due to following reasons. First, the concentration of carcinogens including tar, nicotine, hydrogen cyanide, benz-anthracene, benzapyrene, radioactive uranium are higher in *bidi* smoke (Phadke *et al*, 1990). Secondly, *tendu* leaf used for *bidi* wrapping is less porous and poor in combustibility than cigarette paper, resulting in higher delivery of carcinogenic compounds (Rahman and Fukui, 2000). Thirdly, *bidi* has to be smoked at a minimum of two puffs per minute to keep it burning, but it is actually smoked on an average with 4.75 puffs per minute as compared to two puffs of cigarette smoking (Gupta *et al*, 1980). Hence, bidi smokers inhale more nicotine, tar and other carcinogenic materials than cigarette smokers. In fact, the tar intake has shown to be thrice with *bidi* smoking as that with cigarette smoking (Mishra and Shaikh, 1984). Apart from cigarette smoking, the cigar/pipe smoking has been shown to have a synergistic interaction with alcohol for causing upper aerodigestive tract cancers (Vineis *et al*, 2004). Although cigarette smoking is a recognized predisposing factor for laryngeal cancer, in the absence of tobacco use, the alcohol as such was not found to increase the risk for laryngeal malignancy that otherwise would synergistically enhance the risk for cancer (Lowry, 1975). Warthin's tumor of salivary gland has been strongly associated with cigarette smoking (Pinkston and Cole, 1996). It has been shown (Baker *et al*, 2000; Shapiro *et al*, 2000) that cigar and/or pipe smoking is strongly and casually related to cancers of oral cavity, oropharynx, hypopharynx, larynx and esophagus. In India, modified pipe smoking is seen in terms of indigenous *hookah* and *chillum* use. It is worth noting that reverse smoking of *chutta* seems to have no significance for development of cancer of larynx apart from hypopharynx, esophagus and nasopharynx (Reddy *et al*, 1975).

Number of betal leaf (*pan*) chewed per day by an individual is reported to be high (15–25/day) in Allahabad and Varanasi districts (Mehrotra *et al*,

2003). More so, the special pan from Varanasi called *Banarasi pan* is treated as a delicacy, especially in northern parts of the country. Betal nut chewing alone is rare in Allahabad, although very prevalent in Agra and Mainpuri belts (Wahi *et al*, 1965) of Uttar Pradesh. Furthermore, chewing of *dohra*, an indigenous preparation of tobacco with slaked lime in and around Allahabad, is one of the major factors for the high incidence of this oral malignancy. In north eastern parts of the country, mainly Bihar, *khaini* tobacco as mentioned earlier is usually placed on the inner side of the lower lip within the gingivo-labial groove. About 58% of the users (Stich *et al*, 1982) move the tobacco towards left or right side within the oral cavity whereby carcinogens percolate admixed with saliva to cause irritation of the adjoining mucosa and tongue. It may be possible to have more predisposition of lateral boarder of tongue compared with tip, as it is relatively less mobile and with larger surface area and hence more exposed to the carcinogen mixed saliva.

There are innumerable types of chewable tobacco and related products manufactured in the country with different names (Table 5). The betal quid substitutes are basically a flavored and sweetened dry mixture of areca nut, catechu and slaked lime with tobacco (*Gutka*) or without tobacco (*pan masala*). Even the latter is known to contain substantial amount of nicotine.

Tobacco-specific carcinogens, viz. nitrosamines, nitrate, nitrite and nicotine in these products vary widely. Different brands of a similar type of product usually contain similar levels of specific ingredients as they are influenced greatly by manufacturing process of smokeless tobacco (Brunneman *et al*, 1982). Stepanov *et al* (2005) observed the highest level of tobacco-specific nitrosamines to be present in '*khaini*' that happens to be a mixture of tobacco, lime and menthol or aromatic species. The mode of tobacco processing, favoring the reduction of nitrate to nitrite (and other nitrosating agents) seems responsible for the high levels of nitrosamines. Correspondingly, a high level of nitrite was seen in '*khaini*', probably the highest amongst the smokeless tobacco (Hoffmann *et al*, 1995). Hence, as *khaini* is usually placed in the mouth and retained there, an extremely high amount of nitrite as well as additional amounts of *N*-nitroso compounds formed endogenously will impact the oral mucosa. Increased levels of tobacco specific nitrosamines in saliva of *khaini*-tobacco chewers have been reported (Stitch *et al*, 1992).

Zarda, another smokeless tobacco product, contains relatively high tobacco-specific nitrosamine levels and is produced by boiling tobacco leaves in water with lime and spices until evaporation. A special mention of *Gai chaap* brand that is produced from unprocessed tobacco has been found to contain very high levels of tobacco-specific nitrosamines; this indicates that factors other than the processing may influence the nitrosamine levels as well. *Mishri*, a powdered tobacco primarily used for cleaning teeth, is prepared by baking tobacco on hot metal plate until it becomes uniformly black and nitrosamine uptake is likely to be enhanced if used several times a day. *Gutka* contains less nitrosamine, while *Supari* does not contain tobacco and hence undetectable nitrosamines. Considerable levels of nitrosamines and nicotine have been found in a tobacco containing toothpaste *Dentobac* that is surprisingly marketed in India for dental hygiene, despite its addictive and carcinogenic potential. Considerable levels of tobacco-specific nitrosamines are found in classical Indian chewing tobacco and creamy stuff (Nair *et al*, 1989).

Table 5 Various forms of tobacco-related chewable commercial products in India

Pan masala	*Khaini*	*Tooth paste*
1. Pan parag	1. Raja	1. Dentobac
2. Rajanigandha	2. Hans Chhaap	2. IPCO
Gutka	*Zarda*	*Tooth powder*
1. Tulsi mix	1. Gopal	1. Baidyanath
2. Star 555	2. Manikchand	2. Dabur
3. Zee	3. Goa 1000	*Mishri*
4. Vimal	*Supari*	1. Shahin
5. Manikchand	1. Rajanigandha	*Processed crude tobacco*
6. Kuber	2. Moolchand	1. Hathi chhaap
Snuff	3. Sanket	2. Miraj
1. Click	4. Goa	3. Gai chhaap

Different levels of tobacco in Indian commercial chewing products depend upon the processing technique.

Alcohol use in India

The prevalence of regular alcohol use (4%) in India is lower than previous estimates of 'any' alcohol use (5–7%) in studies from smaller regions of the country (Singh *et al*, 1999; Mohan *et al*, 2002). This study is only a fraction of the reported prevalence of 51% of people reporting alcohol use in USA (US Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, 2003). The regular use of alcohol in India is seen maximum (15%) in fifth decade as compared to second decade (71%) in USA. Neufeld *et al* (2005) have reported other interesting facts related to regular-alcohol-use in India. First, men are 10 times more likely than women; secondly, schedule caste/tribe population is 3.4 times more likely than non-schedule caste/tribe population. Thirdly, those below poverty line have shown greater relative odds for such reporting. Fourthly, the rural population is 1.3 times more likely to report regular alcohol use. Finally, the uneducated class is expectedly more likely to be involved in alcohol abuse. The prevalence of alcohol

Table 6 Prevalence (%) of alcohol consumption in India (1998–1999)

Age group	*Male*	*Female*
15–19	2.4	0.6
20–24	7.7	1.1
25–29	14.9	2.0
30–39	23.6	2.5
40–49	26.1	3.1
50–59	23.9	3.8
>60	18.6	3.1

Adapted from WHO Global NCD Infobase (2002).

consumption as per age is shown in Table 6. Being a poor country, a majority of alcohol users depend upon the crude alcohol manufactured countryside. These local made fermented products are almost always substandard in terms of ingredients and often dangerous/fatal. Wynder *et al* (1956) hypothesized the differences in tobacco and alcohol consumption to be the underlying cause of the differences in the cancer incidence encountered amongst various socioeconomic, educational, cultural and religious groups.

The health impact of many chemicals in the developing country has been underestimated (Pearce *et al*, 1994). For example, a large work force is employed in the construction industry in which substantial exposure to asbestos may occur and there has been a rapid increase in its production in India. Similarly, India is one of the largest producers of silica across the world and occupational exposure to silica dust has been linked to a 2.5-fold increased risk of cancer of salivary gland (Zheng *et al*, 1996). Likewise, for instance, a similar pattern is seen for tyre production with a large increase in its production in developing countries (including India) in 1980s. The risk of salivary gland malignancy is also elevated amongst rubber workers exposed to nitrosamines (Straif *et al*, 1999). The enormous production of tyre especially in north India results in the old and discarded ones being used for manufacturing foot wears. Worst is the impact when tyres are used as a substitute for firewood during peak winter season. The fumes coming out from combustion not only pollute the atmosphere but are potentially carcinogenic. Thus, the number of workers in the industries entailing a carcinogenic risk is increasing in developing countries, partly as a result of the transfer of hazardous industry from industrialized countries. Bhopal gas tragedy is another example when more than half a million people were exposed to toxic methyl isocyanate (MIC) with more than 3000 causalities in 1984.

Solid-fuel-fire cooking and heating stoves used widely in the rural areas have been shown to produce a high indoor concentration of particulates, carbon-monoxide and other combustion-related pollutants. Although the proportion of all such household stoves that are used in poorly ventilated situations is uncertain, the total population exposed to excessive concentration is potentially high. Amongst the work carried out on cancer risk by indoor air pollution, the cook stove smoke has been found to have a little or no risk for nasopharyngeal cancer (Chen *et al*, 1990) in contrast to earlier reports. However, a great deal of work still needs to be carried out to establish the exposure as a risk factor for cancer.

India is primarily an agriculture country and environmental contamination by pesticides has been documented in biotic and abiotic components. These persistent organic pollutants are lipid soluble, non-biodegradable and endocrine disrupters. A study showed that organochlorine pesticides (DDT, DDE, DDD, dieldrin, hepatochlor and HCH) in blood samples were found significantly higher in breast cancer patients (as compared with controls) irrespective of age, diet and geographic distribution (Mathur *et al*, 2002). Although it has not been analyzed for head and neck cancer, the possibility of its impact through aero-digestive route of entry cannot be denied. Hence, it may have still more strong association with head and neck cancer.

The poor socioeconomic status in India predisposes to adulteration malpractices in food. The commonest consumable food item, especially amongst children, is milk. The media has reported its contamination with DDT, HCH, arsenic, cadmium and lead, while liquid soap is often added as a thickening agent and earthworms to render milk more viscous and slimy. These days, fish is treated with chemicals (mercury) to preserve it longer; carbide is used to ripen mangoes uniformly and its exposure is carcinogenic. Similarly, grapes and oranges are also exposed to pesticides and ultimately a portion of these pesticides naturally ends up in drinking water. Goldbohm *et al* (1996) found no link between tea consumption and protection against cancer, whereas adulteration of tea in India with colored sawdust, foreign leaves and exhausted tea leaves is likely to cause cancer. Likewise, adulteration of edible oils and fats by petroleum fractions and white oil is again carcinogenic. Other adulterated food items include mustard seeds (by Argemone seeds), poppy seed/black pepper (by colored foreign seeds), food grains and pulses (by sand grain, marble chips, stones), kesari dal (by *Lathyrus sativus*), turmeric (by lead chromate), apples sprayed over by lead arsenate, food contaminated by rat poison (barium carbonate), and fruit juices/soft drinks in contact with cadmium-plated vessels. Cancer is becoming the biggest killer disease in Kerala and the likely reasons are the large-scale food adulteration and the widespread use of pesticides. In India, consumers are in a big dilemma as they do not have any choice and there is no easy way to detect adulteration.

Selected practices in different regions of India

Eastern India

The high incidence of nasopharyngeal cancer in 'Naga' race is thought to be due to various environmental factors other than racial and prevalent infection by EB virus. It is observed that most of the Naga people live in ill-ventilated houses without separate kitchen, especially in rural areas. They keep fire wood (mainly oak and pine tree wood that produces thick smoke) burning during day and night for heating, lighting and cooking purposes. A bamboo shelf hanging over the fire place is used for smoke drying of meat and vegetables for preservation. They consume this smoke dried food stuffs. The people living in ill-ventilated houses inhale smoke continuously for longer duration compared with those living in well ventilated houses. Such living and dietary habits may play a role in cancer etiology (Kumar *et al*, 1996). The presence of nitroso-dimethylamine (NDEA) in smoke dried meat strengthens the view that consumption of smoked meat may be a risk factor in Nagaland (Sarkar *et al*, 1989). Analysis of soot obtained from roofs of hut-contained carcinogens as well. The use of herbal medicines in this region of the country is suggested to enhance proliferation of EBV-transformed cell and

thus predisposing to nasopharyngeal carcinoma (Hildesheim *et al*, 1992).

On the other hand, eastern part of the country including Assam is famous for housing tea farms. The green tea, as investigated by the researchers, has been shown to contain polyphenols that act as powerful antioxidants against cancer in general.

Groundwater contamination with major outbreaks of arsenic poisoning has been reported from West Bengal (Mandal *et al*, 1999; Chaudhary *et al*, 2000a,b). This happens to be the second worst region after Bangladesh in terms of magnitude among 20 countries in the world (Rahman *et al*, 2003). A WHO report predicts that within a few years, death around these regions could be from the cancers triggered by arsenic. The massive extraction of groundwater for irrigation has so altered the aquifer beneath West Bengal that even deep tube wells are now unsafe in many arsenic contaminated areas. The current intensive efforts to provide deeper wells for safe drinking water are somewhat counterproductive as deep aquifer is simultaneously depleted by irrigation demands on these newer wells. A sector of less educated population has accepted this arsenic calamity as a divine curse and hence needs to be reassured accordingly. Children are more susceptible which means that a whole new generation is at risk. Unfortunately, arsenic infests many areas of West Bengal that has been blessed with numerous rivers, flooded river basins, ox-blow lakes, wetlands and receives about 1600 mm rainfall annually. Hence, without proper water shed management, the condition is likely to worsen further in near future. Spallholz *et al* (2004) hypothesized poor dietary selenium intake as an underlying factor for arsenicosis and cancer in west Bengal. Although the current literature does not provide any substantial data on selenium content of foods within the Ganges-Brahamaputra delta except some older data on selenium bioavailability of local rice (Bieri and Amand, 1976) to be much less (in animal assays) than the US rice. It is worth mentioning about a new challenging concern of increasing arsenic content of food in West Bengal due to irrigation with arsenic-contaminated water (Roy Chawdhary *et al*, 2002). A survey in Kolkata revealed 27.5% of adult men and 18% of women as ever chewers of tobacco (Sen *et al*, 2002). As the incidence of oral cavity cancers in both males and females in Kolkata is low as compared to other regions of the country, it seems to be due to the low prevalence of tobacco chewing in Kolkata compared to other regions in India: 56% in Mumbai, and 40% in Ambillikai (Tamil Nadu) (Gupta, 1996; Rajkumar *et al*, 2000).

Powdered tobacco (*Khaini*) with addition of lime is commonly used by residents of Bihar (Stich *et al*, 1982). The tobacco/lime mixture is usually placed on the inner side of the lower lip within the gingivo-labial sulcus. Such mixture is used for most part of the day and sometimes left at the site during night/sleep. Accordingly the Khaini cancers develop mainly at the site. Poor population uses it as a cheap substitute for the more expensive brands. These are the ones who smoke *bidi* as the least expensive smoking modality.

North India

Kashmir lies in the extreme north, where cancer of esophagus is the most common type of cancer in both genders, a strikingly different finding from the rest of the country (Dhar *et al*, 1993). The epidemiology of esophageal cancer in Kashmir has been found to be similar to 'Asian esophageal cancer belt'. Preponderance of esophageal cancer was attributable to the practice of drinking boiling hot salted tea. Salted tea prepared in Kashmir by adding sodium bicarbonate shows high methylating activity (equivalent to 3 p.p.m. *N*-methylnitrosourea) upon *in vitro* nitrosation (Kumar *et al*, 1992). Siddiqi *et al* (1992) showed a high risk of esophageal cancer in population exposed to aliphatic amines and nitrate from the most commonly used fresh and sun-dried vegetables, red chilies and a widely consumed beverage, the salted tea. There is a high consumption of boiled Brassica vegetables, a rich source of nitrates. Similarly, the prevalence of using smoked fish, sun-dried spinach, sun-dried pumpkin and dried mixed vegetables, which are shown to be rich sources of *N*-nitrosamines, is a probable etiologic factor in esophageal cancer (Siddiqi *et al*, 1991). Moreover, a preliminary survey (Siddiqi *et al*, 1988) shows a widespread contamination of *N*-nitroso compounds in raw foodstuffs from Kashmir. This probably depicts the microenvironment and micronutrient status of the soil.

However, cancers of the oral cavity, larynx, pharynx (and uterine cervix) in north most India have been shown to have a very low incidence (Shah and Jan, 1990). This correlates with the reduction in the incidence of tobacco use from the rest of the country. A unique practice amongst Kashmiris is to use a *kangri* to keep themselves warm. A *kangri* is an earthenware portable charcoal brazier used during winters in Kashmir worn under a loose gown. Although head and neck malignancies have not been attributed to this device, certainly a squamous cell carcinoma of skin is well known to occur on the surfaces constantly exposed to intense heat by prolonged use of *kangri*. The pink to dark reticulated serpiginous patches preceding burns and ulcers subsequently transform into a superficial spreading, ulcero-fungating indolent growth having a potential for loco-regional spread. Fishbein (1993) hypothesized thermal injury and possible interplay of combustion emission products (methane, nitrogen oxide, carbon monoxide, carbon dioxide, methyl chloride, PAHS) including submicron carbonaceous particles (soot) or non-carbonaceous particles (silica) may be involved in altering the structure and function of the cell. It is also possible that submicron particle may make an impact in head and neck area. This impact may, however, be low as the kangri is mostly kept under the gown and seldom near the face.

South India

Tobacco-associated head and neck cancers (tongue, mouth, oropharynx, hypopharynx and larynx) account

for half of the male cancers in this population (Rajkumar *et al*, 2000). Chewing of betal quid containing tobacco and *bidi* smoking have been identified as the major risk factors for these cancers in south India (Sankaranarayanan *et al*, 1989, 1990). A recent sample survey indicated that 40% of men and women (above 15 years age) are betal quid chewers and a quarter of males are *bidi* smokers; 6% of men practice cigarette smoking and smoking is uncommon in women (Rajkumar *et al*, 2000). The cigarette smoking in Ambillikai, Tamil Nadu, seems to have a low prevalence as reflected by the lower incidence of lung cancer (Rajkumar *et al*, 2000). Pan-tobacco chewing was an important risk factor, especially in men. Aghi *et al* (1984) conducted an intervention study on the tobacco habits of rural Indian women and reported unique characteristics of south Indian women using tobacco. The typical woman in Kerala is full time housewife who also works in the fields, growing, tending and harvesting paddy. The rural women are somewhat literate, independent and individualistic. She chews tobacco with betal leaf and areca nut, has her own private supply of chewing material and uses it wherever she wants. Her counterpart in Andhra Pradesh is less literate, probably has more children, seems poorer and may chew tobacco, but smokes *chutta* (reverse smoking). Accordingly, the Kerala women have precancerous lesions on buccal mucosa, groove and tongue, whereas Andhra women have, in addition, on the palate.

Nandakumar *et al* (1990) during an investigation on oral cancers from Bangalore revealed a markedly elevated risk in persons consuming *ragi* (*Eleusine coracana,* family graminae) as staple cereal in their diet. There was also some interaction with tobacco chewing as well amongst the local population. Yeole *et al* (2001) have shown that ASR of cancer larynx is lower in Parsi population as compared to non-Parsis.

Thyroid cancers in India are reported to have the maximum ASR in Trivandrum amongst both genders closely followed by Karunagapally amongst women only. Natural background radiation has been observed in Karunagapally taluka of Quilon district in Kerala, India due to its known reserve of monazite deposits, which emit gamma radiation. Tomatis *et al* (1990) found equivocal association between risk for cancer and geographic variation in natural background radiation. However, therapeutic radiation, radiation fall-out from nuclear weapons testing and radiations from nuclear accidents have been observed as high risk factors (dos Santos Silva and Swerdlow, 1993; Ron *et al*, 1995). Iodine deficiency leading to goiter predisposes to follicular type of thyroid cancer (Bakiri *et al*, 1998; Hellman *et al*, 2001) and iodine-rich areas (iodine supplementation) have been shown to increase papillary type of thyroid cancer. Accordingly, the costal areas of Kerala with wide availability and hence consumption of sea food rich in iodine probably contributes to predominance of papillary cancer and conversely, the increase in follicular cancer in regions remote from costal areas (Poulose, 1990).

Western India

In a retrospective case–control study (Rao and Desai, 1998) in Mumbai, it was found that *bidi* smoking was a significant risk factor for cancer of base tongue. This was much more prevalent than cancer of oral tongue which in turn was linked with cigarette smoking. Also non-vegetarian diet and alcohol were shown to be significant risk factors amongst this population.

In Gujarat, the most common habit in patients of oral cancer was smoking tobacco alone or in combination with chewing *pan-supari* (Malaovalla *et al*, 1976). The possible environmental risk of nuclear explosion of 1974 in western Rajasthan was linked to a high incidence of oropharyngeal and hypopharyngeal malignancies in males (Sharma *et al*, 1992). Considering a long latent period in cancer development following radiation exposure, a possibility of its impact even at present cannot be ruled out completely. In this area, however, lack of investigational facilities and trained personnel, tough working conditions, extremes of temperature, long distances in the desert area with associated poverty, illiteracy and ignorance may be some of the factors responsible for the majority of patients presenting in advanced stages of cancer. Yeole and Jussawalla (1990) reported an exiting fact that men are more frequently addicted to the habits of etiologic importance than women probably explaining the wide variation in male cancer rates for certain sites viz. buccal mucosa, esophagus, tongue, larynx, hypopharynx and oropharynx. Jayant and Yeole (1987) reported a change in bidi smoking habit in the population of Mumbai, while analyzing the declining trends of cancer of tongue, oropharynx and larynx in men. However, they also suggested an emerging cancer pattern in the country at variance with the pattern expected from the current cancer trends in Mumbai. In general, amongst the wide variety of prevalent tobacco habits, bidi smoking, tobacco chewing and cigarette smoking in that order account for a large majority of these cancers (Sanghvi *et al*, 1989).

North-central India

Most of the cancer-related studies represent southern parts of the country; the central-north part is relatively less studied. The use of smokeless tobacco is on the rise in north India and especially in the state of Uttar Pradesh (Mehrotra *et al*, 2003). Chewing of *dohra* is prevalent around Allahabad contributing to oral cancer, whereas betal nut chewing is responsible for oropharyngeal malignancies in Agra and Mainpuri belt (Wahi *et al*, 1965).

The sub-Himalayan region of the country is iodide-deficient, which is known to have a wide spectrum of thyroid disease. The Tarai area has the highest incidence of goitre and also carcinoma of thyroid in north-central India (Varma, 1999). The area of Tarai extending from Gorakhpur in east through Basti, Gonda, Baharaich, Lakhimpur Kheri, Sitapur, Pilibhit, Bariely, Moradabad and Nainital district in northwest is endemic. In non-endemic areas like Agra, Etawah, slightly higher incidence of papillary carcinoma is reported over follicular

carcinoma and the reverse is true in endemic areas (Sarda and Kapur, 1990).

A study carried out by Tariq *et al* (1995) at Lahore (Pakistan) may reflect in part about the surrounding environment of Punjab province. They studied the blood levels of the trace elements and their compounds that are widely distributed in air, water and soils and therefore human exposure is important either directly or via vegetables and animals. They found cadmium and nickel concentrations to be higher in the blood of the cancer patients compared with those in the blood of controls, while copper level in cancer patients was found to be increased in men, but decreased in women.

Madhya Pradesh, the largest central province of the country, is well known for a tragedy in its capital by MIC gas leakage from a Union Carbide Factory in 1984. MIC is an extremely toxic and highly reactive gas (Bucher, 1987). On hydrolysis, MIC gives off mono-methyl amines that in turn can yield nitrosamines (Brown *et al*, 1987). Although marginally increased risk for oropharyngeal cancer has been observed, considering the long latent period of induction of cancer, the full potential of excess risk (if any), is likely to manifest only after 15–20 years.

Due to gross illiteracy in rural areas of Uttar Pradesh, there are some false beliefs amongst the masses that primarily contribute to the late patient presentation at the cancer center. These are 'cancer as a curse', and 'ill-fated to have cancer' as defined by a study from Lucknow (Kumar *et al*, 2001). That the cancer progresses rapidly once touched (even biopsy) is another widely prevalent misconception in a large section of society. This keeps them away from opting for any treatment in the initial stages.

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