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Risk Factors Associated with Lifestyle Cancers in India: A Systematic Review of Existing Evidences from Varied Geographical Locations

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Abstract

Lifestyle cancers are becoming major cause of global morbidity and mortality. India is a country of diverse culture and dynamic life-style which shows variations from one geographical location to another. Evidence suggests that 70% to 90% of cancers in India are related to lifestyle and can be easily prevented by adapting healthier life styles. Thus, this review aimed to examine risk factors of lifestyle cancers in different geographical locations in India. Three electronic databases, namely Psych INFO, JSTOR and Medline were systematically screened from December, 2017 to February, 2018 for literatures on cancer and lifestyle risk factors. The search was limited to India, adults and papers written in English. 2,301 articles were identified and 10 were reviewed. Smoking and tobacco consumption were strongly related with lung, gastric and oral cancers in South and West India. Additionally, in West India, tea consumption was identified as a contributory factor for esophageal cancer while consumption of cabbage and sprout were found to lower the risk of colorectal cancer. In North India, attributions to esophageal cancer were snuff, smoking, salty tea, hookah, sundried foods and red chilli. A number of risk factors were unique to the different geographical locations in India. Awareness of these risk factors would help in strengthening preventive interventions which would facilitate a decline in cancer incidence in India and other countries where similar risk factors are prevalent. This review proposes to organize tailor-made awareness programs reflecting resonance to socio-cultural practice of people to reduce cancer incidence. Also, facilitation of tobacco and smoking cessation programs and strengthening of policies are strongly recommended to strengthen preventive interventions and reduce cancer incidence.

Keywords: Lifestyle; Cancer; Risk factor; Dietary patterns; India; Tobacco; Smoking

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Introduction

Cancer is a lifestyle disease which is grouped according to the location of the cancerous stem cells. The World Health Organization defined cancer as "a generic term used for a large group of diseases that are characterized by the growth of abnormal cells beyond their usual boundaries and can invade to adjoining parts of the body) [1]. Cancer is reported to be the second leading cause of death globally which accounted for 8.8 million deaths in 2015 [2]. The burden of diseases is doubled in the developing countries in that both non-communicable diseases and communicable diseases contribute largely to morbidity and mortality, and India seems to fall in this category where the burden of non-communicable diseases and communicable diseases are 63% and 37%, respectively [3]. The WHO Cancer Country profile revealed that 19.1% of premature deaths from NCDs (3,022,150) in 2016 resulted from cancer [4]. In addition, WHO cancer country profile, also revealed an increase in cancer mortalities from 683,800 deaths in 2014 to 784,821 deaths in 2018 which implies the increasing trend in cancer mortalities in India [4,5]. Anand et al. [6] opined that only 5% to 10% of all cancer cases can be attributed to genetic defects, while the remaining 90% to 95% have their roots in the environment and lifestyle which includes cigarette smoking, diet, tobacco consumption, alcohol consumption, sun exposure, environmental pollutants, infections, stress, obesity, and physical inactivity.

In India alone, about 800,000 new cases of cancer are estimated to occur every year with stark variation across region where the age-adjusted incidence rates in men vary from 44 per 100,000 in rural Maharashtra to 121 per 100,000 in Delhi [7]. The major cancers in men are mostly tobacco-related namely lung, oral cavity, larynx, esophagus, and pharynx. In women, the leading cancers sites include are cervix, breast, and ovary cancer and those related to tobacco namely oral cavity,

esophagus, and lung [7]. India has the largest number of oral cancers in the world, due to the widespread habit of chewing tobacco [8]. Also, India is a nation with wide diversity in food habits and cultural practices, some of which are also found in other countries of the world. The prevalence of lifestyle cancers in India therefore gives a reason to critically examine the risk factors associated with these cancers for the management of lifestyle cancer incidence in India and the world at large.

Methodology

Literature selection criteria

A computerized search for literature was conducted using electronic databases namely Medline through Pubmed, Psych Info and JSTOR. The broad search term used for this review was 'cancer' which was combined with keywords 'prevalence', 'epidemiology', 'burden', 'quality of life', 'health care services', using 'AND' as Boolean operator. Each combination was carried out individually to get maximum results. In addition, MeSH term for cancer i.e. 'neoplasm' was also used for each combination to cover maximum results. All search results were limited to studies with humans and published in English language. To retrieve more recent literature, a timeline of 10 years was traced for database search but in case of JSTOR, timeline of only last five years was retrieved owing to huge nature of JSTOR.

Since lifestyle behavior is mainly formed in adult life, thus present review focuses on cancers among adults leaving children out of the scope of selection procedure. Thus, inclusion criteria for identifying the studies for this review included:

1. Research papers only, review papers or conceptual articles were excluded
2. Cancer as main disease, cancer as co-morbidity was excluded
3. Cancer among adults, studies with children were excluded
4. India as nationality and residency, studies with non-Indians and migrant Indians were excluded.

Data extraction process

Identification of studies for this review involved four stages. At the first stage, a total of 2,301 studies were retrieved from three databases using above keywords, out of which 1,402 were irrelevant to present review since these were pharmacological studies, molecular studies, genetic studies or studies conducted outside India. In addition, 167 duplicates were manually removed by the titles resulting in 732 studies to be screened by abstract.

At the second stage, 732 papers were screened with abstract reading, out of these 617 studied either children or elderly subjects, focused cancer as comorbidity, conducted with non-Indians or migrated Indians. This resulted in 115 studies after abstract screening to be reviewed for full text availability.

At the third stage, all the selected 115 studies were searched for full text availability but only 82 studies were available in full text to download excluding 33 studies from the scope of this review. Further, another 67 studies were removed because they combined children and adult population, focused on lesions, or were review papers which were not clear from abstract reading. Another 5 duplicate studies that were previously omitted were manually removed at full text reading resulting in 10 studies eligible for this review. The selection procedure of eligible studies is presented in Figure 1. Step 1 & 2 was first conducted by DK which was then reviewed by TB & AK. Step 3& 4 were conducted by DK and TB together.

Data from selected 10 studies were extracted using a self developed data extraction form (Table 1) which presented information like year of study, location, age group, duration of study, study setting, objectives, study design, sample size, sampling strategy, analysis procedure and results to facilitate transparency in data analysis. DK extracted data from selected studies. TB and AK then assessed a 30% sample of randomly selected studies to check accuracy and ensure rigor in data extraction process. We differed at few instances in methodology and findings sections of the reviewed studies but consensus was arrived after discussion.

Results

On the basis of geographical location of the research, the selected studies were grouped into three categories:

1. South India (three studies)
2. West India (four studies)
3. North India (three studies)

We could not find any study from eastern part of India using our search strategy.

Studies from South India

One study from South India reported the clinical profile and epidemiological trends of lung cancer with an emphasis on smoking practices [9]. The data was collected from a sample of 258 lung cancer patients (200 males, 58 females) from January 2003 to December 2007. The age range of the participants in this study was 26 to 77 years. The study reported 60.5% participants were ever-smokers while only 39.5% were never smokers. Among the smokers, 71.8% smoked cigarette while 28.2% smoked bidi. A significant correlation (P=0.0028) was found between advanced age at presentation (>60 years) and those with a history of smoking.

Jayalekshmi et al. [10] reported a cohort study conducted in Kerala on the risk of gastric cancer in relation to tobacco and alcohol consumption. A baseline survey was conducted on every resident of Karunagappally taluk covering 65,553 participants (30 to 84 years) for socio-demographic and other lifestyle-related factors from January 1990 to December, 1997. The face-to-face interview survey was conducted with the help of trained field investigators for each resident using a 6-page, standardized questionnaire which was constructed with specific questions to elicit factors such as household socioeconomic status, religion, education, income, and occupation along with lifestyle factors such as smoking and drinking habits, and dietary practices [10]. The study reported that Bidi smoking was associated with Gastric Cancer (GC) risk (P=0.042). The Relative Risks (RR) comparing current versus never smokers was 1.6 (95% CI: 1.0-2.5). Gastric cancer risk was associated with the number of bidis smoked daily (P=0.012) and duration of bidi smoking (P=0.036). Those who started smoking bidi at younger ages were at an elevated GC risk. The RRs for those that started bidi smoking under the age of 18 and ages 18 to 22 were 2.0 (95% CI: 1.0-3.9) and 1.8 (95% CI: 1.1-2.9), respectively, when their risks were compared with lifetime non-smokers of bidis.

Mahapatra et al. [11] also examined the association between oral cancer risks and consumption of tobacco, cigarette and other oral dip products from March 2013 to July 2013 with 402 participants

Table 1: Summary of reviewed studies.

First Author and Year	Objective(s)	Design	Sample and Sampling strategy	Analysis procedures	Main findings	Reviewer' Remarks
Krishnamurthy et al. [9], 2012, South India (Chennai)	To analyze the clinical profile and the epidemiological trends in lung cancer patients with an emphasis on the smoking practices from a single tertiary care center	5- Year Retrospective-prospective study on 258 lung cancer patients (200 males, 58 females) aged 26-77 years in a tertiary health setting in Chennai.	Retrospective analysis of prospectively collected data of consecutive hospital in-patients with a proven diagnosis of lung cancer at a tertiary care oncology centre.	SPSS software (Version 18) was used.	60.5% were smokers while 39.5% were non- smokers. Smokers were cigarette (71.8%) and bidi (28.2%) smokers.	Single facility study which may not represent the general population Sample size determination was not reported.
					Adenocarcinoma was most prevalent among non-smokers (52.7%) and squamous cell carcinoma among smokers (80.4%).	Study included survival rate of the sample.
					Significant correlation of smokers presented at advanced age (>60 years) with squamous histology compared to adenocarcinoma histology (P=0.0028).	Structured abstract
Ganesh, et al. [10], 2009, West India (Mumbai)	Evaluating the association of some life-style factors, dietary items on risk of esophageal cancer.	3-year hospital-based Case control study on 2,070 participants (442 cancer cases, 1628 controls) aged 30-75 years in Mumbai. Cancer site is esophagus. Questionnaire and interview was used for data collection	Interview of patients at Out-patient department of the hospital prior to diagnosis, record of information into pre-designed questionnaire, segregation of subjects into 'cancer cases' and 'controls'.	Univariate analysis and Unconditional logistic regression was applied using SPSS Version 15.0 software	Tobacco+ pan chewers have 1.3 times excess risk (OR=1.3).	Unstructured abstract.
					Smoking bidi increased the risk 1.8 times (OR=1.8) and smoking cigarettes increased the risk (OR=2) 2- fold. Alcohol drinkers had an 1.8-fold increase in risk (OR=1.8).	Research design was clearly presented which makes replication of the study possible.
					Fresh fish consumption showed protective effect (OR=0.8). Consumption of tea showed a 4-fold increase in risk (OR=4.0). positive dose-response relationship in pan+ tobacco chewing, cigarette and bidi smoking	Dietary pattern of the population
						Location of residents outside Mumbai was not mentioned.
Sehgal et al. [11], 2012, North India (Jammu)	To identify the risk factors of esophageal cancer and study their effect on the survival rates patients of Jammu region, India.	Hospital –based Case control study on 200 case control pairs aged 34-80 years. Study was from Oct.2007 to July 2011 in Jammu. Cancer site is esophagus. Short-structured questionnaire was used for data collection	Sample was selected from patients attending the Endoscopy Unit of Government Medical College, Jammu	EORTC protocol. Univariate logistic regression analysis, Chi-square test, independent Student's t-test. Multivariate logistic regression analysis and Kaplan-Meier survival curve EORTC protocol. Univariate logistic regression analysis, Chi-square test, independent Student's t-test. multivariate logistic regression analysis, and Kaplan-Meier survival curve analysis (using Log-rank test) were used	The demographic characteristics of the two groups were not significantly different (P>0.05). However, life style characteristics, dietary characteristics differed.	Sample size determination was clearly stated using the EORTC protocol.
					Logistic regression analysis showed that smoking, snuff, sundried food, red chili and baking soda was significant (P<0.05 or P<0.01 or P<0.001) potential risk factors for esophageal cancer. Snuff showed highest risk, followed by baking soda, smoking, sundried food and red chili.	Research design was clearly
					Association of these risk factors with patient (cases) 3-year overall survival clearly shows that the probability of survival lowered significantly in patients who took snuff, red chili and smoked	Presented informing the possibility of replicating the study.

						3–year overall survival rate analysis was clearly stated using Kaplan – Meier survival curve Analysis
						Structured abstract
Khan et al. [12], 2011, North India (Kashmir)	To identify the risk factors that may have a role in the development of esophageal cancer in Kashmir valley region.	1-year hospital-based case control study on 200 case control pairs aged 38-76 years in Kashmir. Cancer site is esophagus. Data was collected with the use of questionnaire	Sample was purposively collected from patients attend the tertiary care institution.	Not specified	37% of cases and 18% of control are farmers. Among cases, there were 72 smokers and out of these 91% were hookah smokers while in controls, there were 42 smokers, 35.7% were hookah smokers. 78% of cases had smoked more than 20 g of tobacco per day. Cancer of esophagus was found common in females as well. Twenty-nine (29%) of female cases were house wives and were exposed to kitchen smoke and fumes.	Structured Abstract.
					Intake of different varieties of vegetables other than the Haakh was limited. Consumption of fresh fruits was very low. Occupational exposure and smoking, particularly the hookah smoking, are the contributory factors	Sample size determination not mentioned.
						Age range of sample was clearly stated
						Lifestyle data included dietary pattern of the population.
Ganesh et al. [13], 2009, West India (Mumbai)	To determine the various factors associated with colorectal cancer, such as tobacco, alcohol drinking and dietary items	3- Year hospital- based Case control study on 1,831subjects (203 cases, 1628 controls) aged 30-75 years in Mumbai. Cancer site is colon and rectum. Data was collected with the use of questionnaire and interview.	Patients who visited the hospital for diagnosis and treatment were interviewed at the out-patient department of TMH, prior to diagnosis. The information was recorded in a pre-designed questionnaire that included demographic characteristics (age, sex, religion, etc.), life-style (habits such as smoking, chewing, alcohol drinking, etc.), dietary habits and dietary items. Cases were histologically proven cancer cases of colon and rectum and cancer-free patients were considered as controls by scrutinizing their medical history and diagnosis.	Unconditional logistic regression model using SPSS Version 15.0 software.	Cabbage eaters showed a significant reduction in risk. Similarly for sprout eaters, the risk reduction ranged 30% (among women) to 50% (among 'both sexes and men') and was not significant among 'men'. There was no significant risk reduction among those consuming other vegetables. There was an enhanced risk of 1.6-fold and 1.0 for dry-fish eaters among men and women respectively while there was a 40% reduction for fresh fish-eaters.	Research design was detailed thereby making replication of study possible.
					No excess risk was observed for smokers, alcohol consumption similarly did not emerge as a significant risk for colorectal cancer.	Only two occupational categories were mentioned (agriculture and non-agriculture), limiting data on occupational risk factors
						Unstructured abstract
Balasubramaniam et al. [14], 2013, West India (Mumbai)	To determine the various factors associated with Non-Hodgkin Lymphoma, such as tobacco, alcohol drinking, dietary items and occupational exposure history.	2-year hospital based Case control study on 1,773 males (442 cancer cases) aged ≥ 24 in Mumbai. Cancer site is lymphocytes. Questionnaire and interview were used for data collection	Patients who visited the hospital for diagnosis and treatment were interviewed at the Out-patient department. The information was recorded in a pre-designed questionnaire, which was pre-tested at the hospital; this included demographic characteristics (age, sex, religion etc), life-style (habits such as smoking, chewing, alcohol drinking etc), dietary habits and occupational exposure	Unconditional logistic regression model was applied using SPSS Version 15.0 software.	Smoking is a high risk factor for Non-Hodgkin Lymphoma (NHL), no excess risk with alcohol drinking.	Only males are included in the Study.

					Red-meat consumption increased the risk seven-fold while fish, eggs and chicken didn't show any excess risk. Coffee drinking showed a 50% reduction in risk, while consumption of milk increased the risk six-fold. Significant relationship (3-fold) was observed with exposure to pesticides.	Age range is not clearly defined.
						Study included data on dairy
						Products and coffee drinking to Dietary patterns.
						Limitations of the study were not reported.
						Structured abstract
Mahapatra et al. [15], 2015, South West India (Karnataka)	To find the association between gutka consumption and oral cancer.	5-month hospital-based Case control study on 402 subjects (134 cases, 268 controls) aged 18-83 years in Karnataka. Cancer sites are buccal mucosa, lateral surface of the tongue, base of the tongue, lip, hard palate. Data was collected by interview using a structured questionnaire	Patients diagnosed with oral cancer receiving treatment at Shirdi Sai Baba Cancer Hospital were included in the study as cases and the patients in the Department of Ophthalmology and General medicine at Kasturba medical hospital during the study period were included in the study as controls	Univariate logistic regression, multivariate logistic regression and SPSS version 16 was used	The respondents who consumed gutka were 5.1 times more likely to get oral cancer compared to people who did not consume gutka. Similarly, the respondents who consumed supari were 11.4 times more likely to get oral cancer compared with people who did not consume supari. Bidi smokers were 2.3 times more likely to get oral cancer when compared to people who did not smoke bidi.	Research design was clearly
	To study the association between oral cancer other tobacco products.					Presented implicating the ability to replicate the study.
						Abstract is structured.
						Aims and objectives of the study are clearly stated.
Madani et al. [16], 2012, West India (Pune)	To investigate the association between tobacco and poly-ingredient oral dip products consumption and oral cancer	Matched hospital-based case control study on 350 case control pairs aged ≥ 18 in Pune. Cancer site is oral cavity. Duration was from Feb. 2005 to Sept. 2006. Data was collected with the use of structured questionnaire	Samples were selected by Scheduled sampling. Cases were patients newly diagnosed with cancer of oral cavity and controls were selected from the relatives, friends and caregivers of the cases, who were accompanied the patients at the hospital and were healthy and did not reportedly have cancer	Univariate analysis, multivariate analysis, Chi-square test of independence of attributes SPSS version 13 were used	The overall smoking and smokeless tobacco as well as drinking alcohol, and non-vegetarian diet habits were significantly different between cases and controls (P=0.001). 3 Smoking categories (filtered, non- filtered cigarette and bidi) were prevalent in cases. Similarly, all the oral dip products {chewing tobacco, mishiri, pan parag, gutkha, supari, and betel quid (paan)} except betel quid, (P=0.112), and panparag (P=0.621), showed significant difference in cases.	Sampling method was reported.
					Risk was 7.3 for consumption of gutkha, 5.3 for consumption of chewing tobacco and 4 for consumption of supari (pure areca nut). Lower risk was found for mishiri. In the case of smoking, only bidi smoking was of a significant risk	Matched case control.
						Limitations of the study were Clearly reported.
						Unstructured abstract
Jayalekshmi et al. [17], 2015, South India (Kerala)	To assess the risk of gastric cancer (GC) in relation to tobacco use and alcohol drinking in the Karunagappally cohort in Kerala, South India	Cohort study in a rural setting conducted on 65, 553 males aged 30-84 years from 1990-2009. Data was collected using interview and questionnaire	Baseline survey was carried out from 1990 to 1997 on Karunagappally cohort	EPICURE program (DATAB; AMFIT). Poisson regression analysis of grouped data and H0 (calendar year, attained age, occupation, and education) exp (β2X2 + β3X3) model.	Bidi smoking was associated with a higher risk of Gastric Cancer (GC). GC risk increased with the increased number of bidis smoked daily (P=0.012) and with a longer duration of bidi smoking (P=0.036). Cigarette smoking or tobacco chewing was not significantly associated with GC risk. Alcohol drinking was similarly not significantly associated with GC risk.	Only males are recruited into the Study.

						Sample size determination was not reported.
						Limitations of the study were stated.
						Structured abstract
Panda et al. [18], 2013, North central (New Delhi)	To evaluate the association between selected demographic, lifestyle, and dietary factors and Gall Bladder Cancer	Hospital --based case control study on 122 case control pairs in New Delhi. Cancer site is gall bladder. Duration was Jan. 2008-Oct. 2009.	Cases were defined as newly diagnosed cases of histologically confirmed Gall Bladder Cancer registered with the gastrointestinal cancer clinic during the study period. Controls were recruited from among the healthy relatives of histologically confirmed Gall Bladder Cancer registered with the gastrointestinal cancer clinic during the study period. Controls were recruited from among the healthy relatives of patients other than Gall Bladder Cancer registered at the same center without any known gall bladder disease.	Epi-Info version 6, SPSS version 15, chi-square test, t-test, Multivariate logistic regression was used	No significant difference in age and sex between the cases and the controls. In the bivariate analysis, factors found to be significantly associated with Gall Bladder Cancer were illiteracy, lower socioeconomic status, and parity more than 3, age at first pregnancy less than 20 years, and the use of non-liquefied petroleum gas cooking fuel. Higher vitamin C intake had a protective effect.	Matched case control
		Data was collected with the use of semi-structured interview schedule, food questionnaire, modified kuppuswami scale and Uday Parikh scale			In the multivariate analysis, education, intake of vitamin C, parity, and type of fuel used were significant factors.	Sample size determination was reported.
						Research design was clearly reported implicating replicability of the study
						Unstructured abstract

(134 cases, 268 controls) in Karnataka. The study reported that the risk of oral cancer is associated with smoking, smokeless, oral dip products, gutkha and other tobacco products. They also reported a preponderance of males (82.8%) over females (17.2%). Majority of the cases consumed gutkha (35.8%), 14.9% consumed supari, 20.1% chewed tobacco, 17.4% consumed betel quid, 9.7% used snuff, and 70% consumed alcohol daily. They further reported the odds of oral cancer in cases that consumed gutka, supari, tobacco, betel quid, bidi and alcohol to be 4.8, 6.5, 7.3, 3.2, 6.9, 2.1 times higher than those that do not consume these products respectively. Conversely, there was no association between mishiri, betel quid, smoking cigarettes and the risk of oral cancer.

Studies from West India

Ganesh et al. [12,13] conducted two 3-year long studies (1989 to 1992) in Mumbai on esophageal cancer (N=2,070; 442 cases, 1,628 controls) and colorectal cancer patients (N=1831; 203 cases, 1,628 controls). They studied the risk of demographic, dietary habits and lifestyle factors through interview in an out-patient department. These examined tobacco, alcohol, unhealthy diet and tea drinking as risk factors of esophageal cancer and colorectal cancer in Mumbai. They reported a moderate 1.3 times excess risk for chewers of pan (betel-leaf) with tobacco, 1.8-fold excess risk each for bidi smokers and alcohol drinkers, 2-fold for cigarette smokers, and tea drinking showed a 4-fold excess risk for esophageal cancer. Both studies also reported a dose-response relationship among pan with tobacco chewers and an increased risk with time duration. Similarly, bidi and cigarette smoking showed a positive dose-response relationship where the risks increased to 2.4 and 2.5 folds respectively. Some significant findings emerged regarding the dietary habits and colorectal cancer. Cabbage-eaters had a 50% reduction in risk among both the genders, compared to those who did not eat cabbage. Sprout eaters also had a 30% to 50% reduction in risk. There was an enhanced 1.4-fold risk among 'dry-fish' eaters compared to non-eaters. Among women, meat-eaters had a 2.4-fold excess risk than non-meat-eaters. Dark-green-leafy-vegetables did not show any protective effect for colorectal cancer [12,13].

Madani et al. [14], between February, 2005 and September, 2006 examined the risks of oral cancers with consumption of tobacco, cigarette and other oral dip products in Pune. A matched case-control sample (N=700; 350 controls, 350 cases) was studied using a self-reported questionnaire tracking information on consumption of tobacco, poly-ingredient oral dip products, alcohol, dietary habits and demographic status. A great risk of oral cancer in tobacco chewers and oral dipping consumers was reported. Three Smoking categories (filtered, non- filtered cigarette and bidi) were prevalent in cases and all the oral dip products {chewing tobacco, mishiri, gutkha, and supari} except betel quid, (P=0.112), and panparag (P=0.621), showed significant difference in cases. The study reported an increased risk amongst bidi smokers but no significant effect of betel quid and filtered cigarette on oral cancer risk [14].

Balasubramanian et al. [15] reported the risk factors for Non-Hodgkin lymphoma in Mumbai (1997 to 1999) with male subjects only (N=1,773; 390 cases, 1,383 controls) through a pre-designed questionnaire [15]. The study examined the significance of alcohol, tobacco, dietary items and occupational exposure to non-Hodgkin lymphoma risk. The findings suggested that, among the dietary items, only consumption of mutton showed 7.0-fold significant excess risk for non-Hodgkin lymphoma. Consumption of milk showed a 6-fold excess risk (OR=1.5); while coffee showed a 50% reduction risk for non-Hodgkin lymphoma. Among occupational factors, exposure to pesticides showed 3-fold excess risk for non-Hodgkin lymphoma.

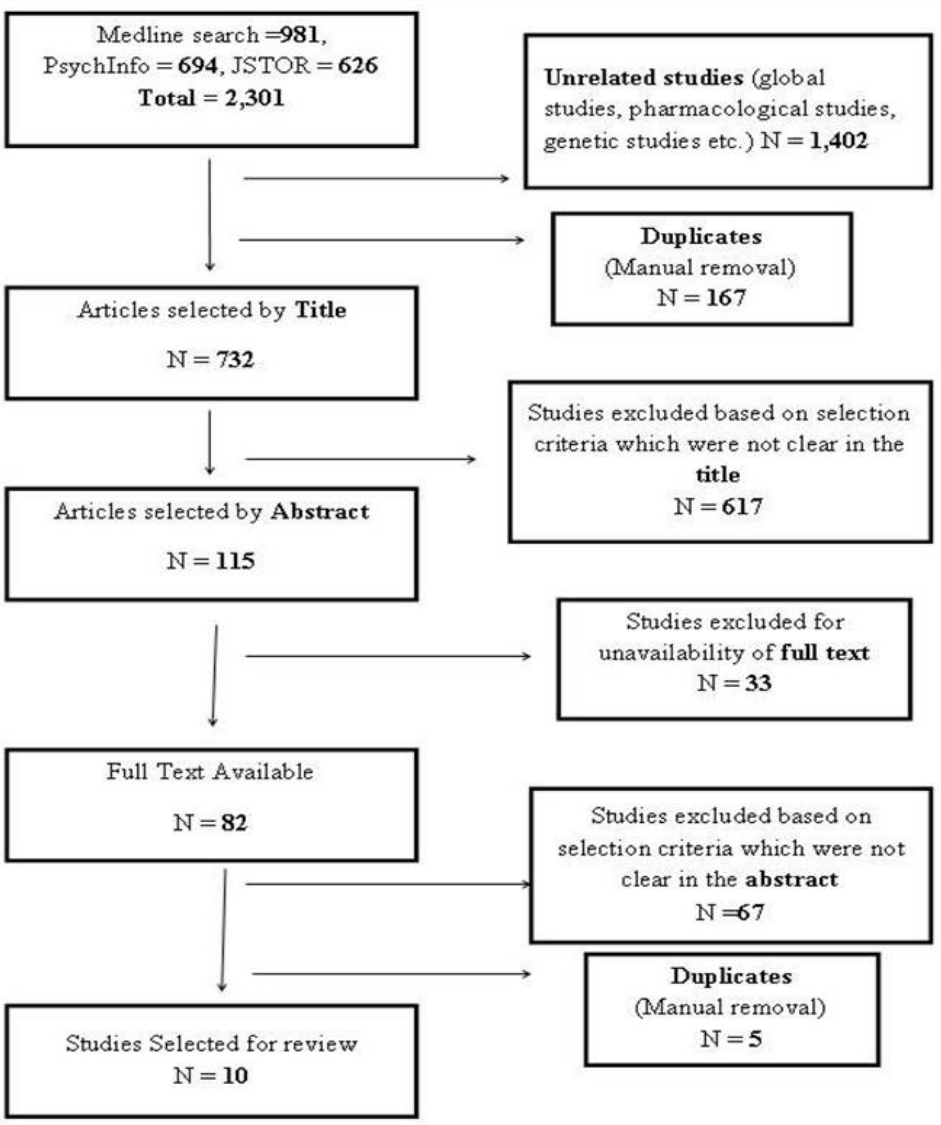

Figure 1: Flow chart representing selection procedure of the reviewed papers.

Studies from North India

In North India, Sehgal et al. [16] reported the risk factors of Esophageal Cancer (OC) in Jammu (N=400; 200 cases, 200 controls). Samples were selected from patients who attended the Endoscopy Unit of Government Medical College from October 2007 to July 2011. Patients below the age of 80 years and being diagnosed with squamous cell carcinomas of the esophagus were the cases while patients diagnosed with other diseases were the controls. Data on age, gender, educational level, and socio-economic status, family history of OC (first-degree relatives), clinic pathological symptoms and dietary habits were collected using a short-structured questionnaire. The study examined risk factors and survival rate of OC and revealed that among dietary characteristics, snuff was highest (OR=3.86, 95%) followed by salt tea (OR=2.53, 95%), smoking (OR=1.97, 95%), sundried food (OR=1.77, 95%) and red chilly (OR=1.76, 95%). The probability of survival also lowered significantly among those consuming tobacco in the form of snuff and smoking as compared to those who did not take these [16].

Also, Khan et al. [17] conducted a study at a tertiary care institution in Kashmir from January to December, 2008 with a sample of 100 diagnosed patients of esophageal cancer (cases) and 100 healthy individuals (controls). A predesigned questionnaire covering personal, occupational, dietary and family history was administered. A preponderance of male cases over females was reported and majority of the cases were farmers (37%) and house-wives (29%) belonging to the low-socioeconomic status. It was further reported that, 91.7% of the cases were hookah smokers (major mode of smoking in Kashmir), 78.8% smoked more than 20 g of tobacco per day, and 24% consumed five cups of salty tea per day. Sun-dried vegetable called Haakh was consumed by both cases and controls. With respect to fruit consumption, 45% cases consumed monthly, 40% consumed weekly while none consumed fruits daily. Consumption of meat on a monthly, weekly and daily basis was 69%/15%/14% and 44%/42%/14% in controls and cases respectively. None of the groups chewed tobacco or consumed alcohol [17].

The third study is a matched hospital-based case control study (February 2008 to October 2009) conducted on the role of lifestyle and dietary factors in Gallbladder Cancer (GBC) in the Northern part

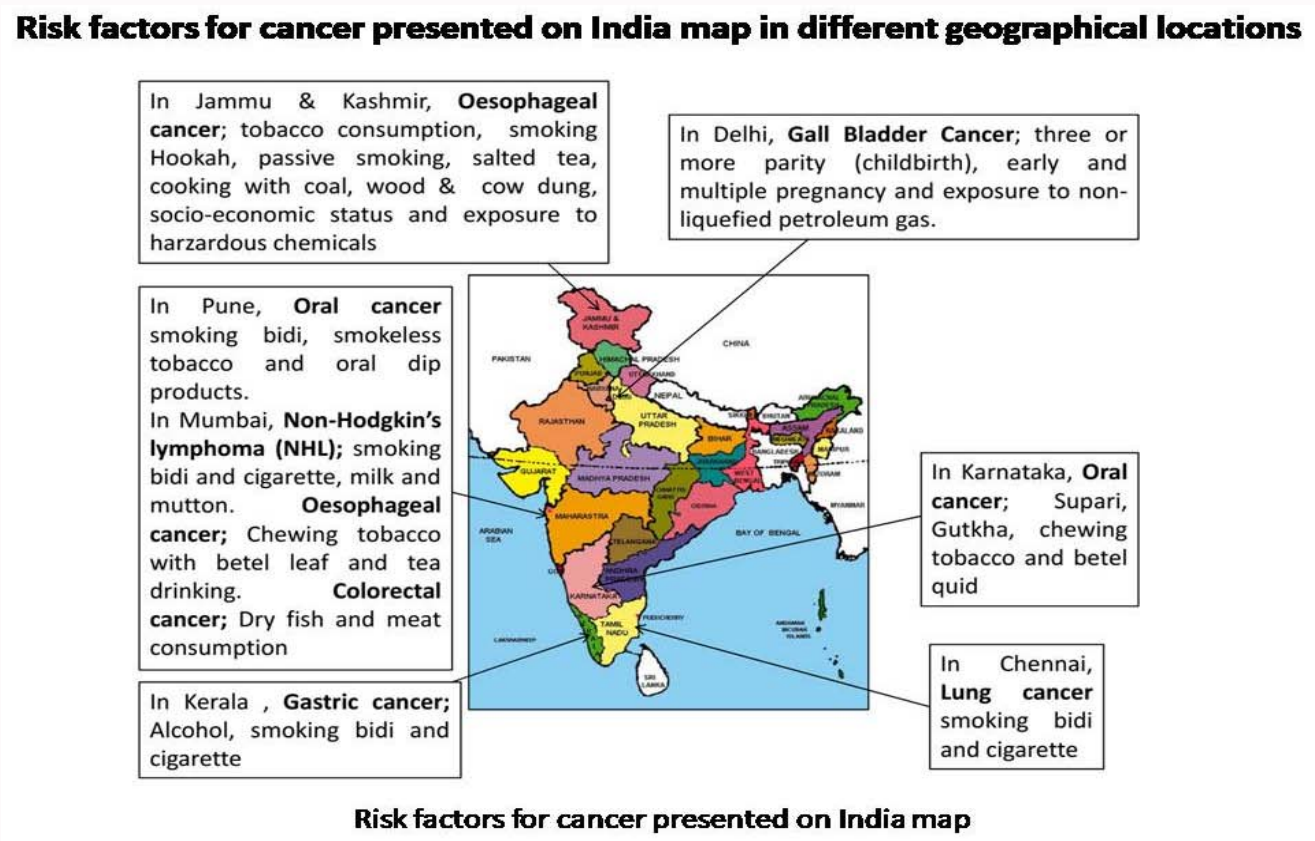

Figure 2: Risk factors for cancer presented on India map.

of India [18]. The study was conducted at the All India Institute of Medical Sciences, New Delhi with a sample size of 244 individuals from Delhi, Uttar Pradesh, Bihar, Uttarkhand, Rajasthan, Punjab, Orissa and Jharkhand. Cases (122) were newly registered confirmed primary GBC patients while controls (122) were healthy relatives of patients. Data were collected using a semi-structured interview schedule. The study revealed that illiteracy, low socioeconomic status, high parity (more than three); early pregnancy and use of non-liquefied petroleum gas are associated with the risk of gall bladder cancer. They further reported that there was no significant relationship between alcohol consumption, tobacco consumption, education and age at menarche. Vitamin C intake was also reported to have a protective effect [18]. Geographical distribution of risk factors has been presented on India map in supplementary file (Figure 2).

Discussion

This systematic review appraised the risk factors for cancer in India. The studies were location-specific with none covering India as a whole. In addition to the commonly known risk factors like smoking, alcohol and tobacco consumption, dietary patterns and life style factors were also identified to pose risk to certain cancers. However, a variation was seen depending upon geographical location and different cancer sites.

Smoking

Smoking has been identified as the predominant cause of lung cancer, esophageal, oral and gastric cancer across the world having increased risk with longer duration and high quantity of consumption [9]. Earlier studies have reported a higher risk with bidi smoking in comparison with cigarette [19-21]. High prevalence of lung cancer in Chennai was attributed to smoking (bidi and cigarette) especially among males, and the significant correlation found between advanced age at presentation (>60 years) and those with a history of smoking suggests high risk of cancer among advanced age smokers in comparison to young age [9]. Hookah smoking was quite popular in Kashmir region particularly among farmers. Smoking was also an established risk factor for esophageal cancer [22-25]. In Pune, bidi smoking was identified as a significant risk to oral cancer while betel quid and filtered cigarette were not. Bidi smoking was observed to be more prevalent than cigarette; this could be attributed to the cheap cost thereby implicating its affordability by the low socioeconomic status [14].

In Kerala, higher frequency and increased duration of bidi smoking heightened the risk of cancer and significant differences were observed for gastric cancer incidence among the low socioeconomic class. These differences could be associated to their dietary patterns, although it was not reported in the reviewed study [10].

Cigarette smoking and bidi smoking were reported to be associated with Non-Hodgkin's Lymphoma (NHL) in Mumbai while alcohol consumption was not, although risk was enhanced in drinkers by 50% compared to non-drinkers [15].

Passive smokers

Previous studies have established the association between smoking and lung cancer; nevertheless, there has been a rising trend in the occurrence of lung cancer in non-smokers as well especially among females. This could be attributed to second-hand smoking,

whereby they were exposed to passive smoking from their spouses while they worked closely on the farm and other indoor air pollutants [3,26,27]. This has also been reported as a contributory factor predisposing women to the risk of esophageal cancer in addition to the use of cow dung, wood and coal for cooking in Kashmir [17,28].

Tobacco consumption

Consumption of tobacco has been reported in various forms, such as, cigarette, hukka, bidi and snuff in the Jammu region [9]. In addition to previously established association of cigarette, hukka and bidi with esophageal cancer, snuff intake has also been correlated with esophageal cancer because of the presence of tobacco carcinogens in moist snuff [29].

Over half of all tobacco consumed in India is smoked as bidi (Indian specific non-filtered cigarette) and about one-fourth of tobacco consumption is in smokeless form, such as chewing tobacco and mishiri [30]. A great risk for oral cancer was found in the habit of tobacco chewing, with or without lime, which is kept in the mouth for different durations depending on personal habits. In an investigation that compared smokers with smokeless tobacco and oral dipping products users, both were at increased risk of oral cancer [14]. This could be due to the direct contact of these products with the oral epithelium of the users.

India has the largest number of oral cancer diagnosis in the world, due to the widespread habit of chewing tobacco [8]. Oral cancer is strongly attributed to consumption of gutkha, tobacco chewing, consumption of supari and consumption of mishiri. Areca nut, the seed of the fruit of the oriental palm Areca catechu, is commonly used in India to prepare paan or betel quid, pan masala and gutkha. Chewing of pure areca nut has been associated with the risk of oral cancer because of its ability to promote carcinogenesis [31]. Gutkha contains areca nut, slaked lime, catechu, condiments, and powered tobacco. Gutkha can be highly addictive when compared to chewing ordinary tobacco as it has been previously shown to be a gateway to smoking [32].

When compared with non- consumers, Gutkha consumers were 5.1 times more at risk of oral cancer, supari consumers were 11.4 times more at risk, tobacco chewers were 6.0 times more at risk, betel quid consumers were 6.4 times more at risk and bidi smokers were 2.3 times more at risk of oral cancer while Betel quid had no significant effect in causing oral cancer [11,14].

This could infer a protective effect of betel leaf (the main ingredient of betel quid) to the oral mucosa against the harmful alkaloids in areca nut. Betel leaf is known to be rich in beta-carotene which has the capacity to quench free radical [2].

In contrast, another study opined that chewing tobacco with paan (betel leaf) is more harmful in causing esophageal cancer than chewing tobacco only. It was speculated that while chewing tobacco with betel leaf, the juice comes in contact with the esophagus mucosa as opposed to tobacco juice alone which may be spat out without a direct contact with the esophagus mucosa [13].

Alcohol consumption

Although oral cancer risk was not reported to be associated with cigarette smoking and mishiri consumption but alcohol was reported to be associated with a high risk of oral cancer [11]. In Kerala, Alcohol consumed was limited to arrack because it was the commonly consumed among the study population. Majority of the cases were educated only until primary level and this could have an influence on their heightened alcohol consumption. Future researches are therefore recommended to establish the association of gastric cancer with other alcoholic drinks alcohol drinking was not reported in Kashmir; this could be due to the prevalence of Muslims in the region [33].

Dietary pattern

Tea is a common beverage in India. Salted tea has been reported as a dietary factor which is strongly associated with esophageal cancer [31]. The tea is prepared by brewing green tea leaves with sodium chloride to obtain a reddish brown extract after which water, salt and milk are added to it. Consumption of bicarbonate-containing hot salted tea, commonly consumed by Kashmiri people, has been identified as dietary high-risk factor associated with the development of esophageal carcinogenesis. This type of tea is commonly consumed at a high temperature due to the harsh weather that is prevalent in the region. The hyperthermic effect of this tea could be injurious to the esophageal mucosa [34]. This correlates with an earlier study that reported a relationship between tea drinking and stomach cancer in Kashmir [33].

Also, the risk of esophageal cancer due to tea drinking was reported in Mumbai as a result of the high temperature of the tea consumed, which could be injurious to the esophageal lining, although the actual temperature that causes injury is not known [13]. In contrast, another investigation reported tea drinking to show less risk and coffee drinking showed a 50% reduction in risk when compared to non-drinkers [15]. Coffee has been reported to protect from cancer through the activity of its anti-carcinogenic constituents [35].

In Kashmir region, the diet commonly consumed are cooked rice, green-leafy vegetable called haakh and salted tea. These have limited source of protective factor from esophageal cancer, as compared to the consumption of different varieties of fruits and vegetables, which are rich in the presence of vitamins and carotene that induces anti-oxidant effects [36]. Increased intake of vitamin C was reported to be a protective factor against Gall Bladder Cancer, this is supported by an earlier hypothesis posing vitamin C to be an antioxidant which prevents the formation of carcinogen from precursor compounds, although there is no strong evidence for this [37]. Also, dietary factors revealed red meat consumption to be a high risk factor for the incidence of NHL; this has also been confirmed by earlier studies [38]. However, high consumption of vegetables reduced the risk of NHL but they did not emerge as a protective factor [15]. Fresh fish on the other hand was reported to be a protective factor, this finding is similar to a study reported on risks of esophageal cancers in Mumbai [13,39]. Animal studies have shown that fat from fish contains 20% to 25% saturated fatty acids, and fish and fish oil are a rich source of n-3 fatty acids and the fat-soluble vitamins A and D, and these n-3 fatty acids have anti-inflammatory effects [40].

Meat consumption was found to be a risk factor among the women in the population which could be as a result of their small sample size when compared to the males (females =59, males =144). Further research should be conducted on a larger population in order to establish the association between meat consumption and colorectal cancer in females. Among the vegetarian diets, only cabbage and sprout consumption were reported to be protective factors while dark green leafy vegetables, root vegetables and other vegetables were not shown to reduce the risk of colorectal cancer. The anti-carcinogenic

actions of cruciferous vegetables are commonly attributed to them because they contain glucosinolates [41]. Sprouts contain antioxidants which may be the reason for its protective factor.

Food preservation

Owing to unavailability of vegetables, nomadic lifestyle and harsh weather, sun-drying is a common strategy used to preserve food in Jammu and Kashmir. This method facilitates the growth of mould, fungi and the presence of trace levels of several volatile and non-volatile N-nitroso compounds which have been strongly implicated with esophageal cancer [31,42,43].

Furthermore, the risk of colorectal cancer in Mumbai was associated with consumption of dry fish. This is speculated to be due to the fact that the dry fish is salted, dried and preserved for later use thereby exposing it to harmful microorganisms [12].

Occupational exposure and socioeconomic factors

Occupational exposure was reported as a contributory factor to the risk of esophageal cancer in Kashmir where farmers are likely exposed to hazardous chemicals and biological farming that are suspected carcinogens [17]. Although, the relationship between farming and risk of esophageal cancer was reported, other occupations were not included, therefore studies that include other occupations are strongly recommended. Also, poor socio-economic status posed to be a major risk factor predisposing the population to esophageal cancer in Kashmir. The absence of dietary nutrients, specifically vitamins A, E, C and trace elements like zinc and selenium in meals, as observed in poor people increases the chances of cancer [44,45].

In North India, the risk factors associated with Gall Bladder Cancer (GBC) were low education, three or more parity (childbirth), early pregnancy and exposure to non-liquefied petroleum gas [18]. Early pregnancy and multiple pregnancies will elevate the levels of progesterone and estrogen which may change the lithogenicity of bile and increase the risk of GBC [46]. Non-liquefied petroleum gas does not burn completely therefore producing carbon monoxide, poly-organic and poly-aromatic hydrocarbons and other gases that could be carcinogenic thereby causing harm to women who use them to cook [21]. The role of traditional non-liquefied petroleum gas fuel in the incidence of GBC has not been well established, therefore future research is recommended in this area.

India being a country with a wide variation in food habits and cultural practices infers the possibility of similar lifestyle risk factors in other nations of the world. Consumption of hot tea and smoking are common habits in cold regions where people want to stay warm in the cold seasons. Also, there is a high rate of alcohol and tobacco consumption in many developed and developing countries inferring a high risk of cancer incidence. In addition, meat is a highly consumed non-vegetarian diet in various countries in the world while vegetables are still less consumed in many countries causing poor nutrient intake in the population. These lifestyle risk factors, though are revealed from studies in India have the potential to draw inferences to other countries which have similar life-style.

Major gaps and recommendations

Hospital based surveys might not present the actual prevalence of cancer in the regions, therefore large population-based research is required to reveal the lifestyle risk factors of various cancers in the country for policy based interventions.

Also, occupational exposure history especially exposure to chemicals, poisonous gases, and other occupational hazards needs to be studied with large samples in order to examine the suggesting relationship with cancer. In addition, physical activity which is also a risk factor for lifestyle cancers was not included in any of the reviewed studies.

We therefore recommend future research focusing on physical activity and its association with risk of cancers. In addition, we recommend that future research should examine the evidence of these contributory factors in the risk of cancers in India. Also, we recommend the need for quality research in other parts of India, in order to provide a wider perspective to the lifestyle factors that is contributing to the rising burden of lifestyle cancers in India.

Conclusion

In conclusion, this systematic review reveals that lifestyle cancers have a high incidence in India and this could be associated with the prevalence of risk factors like tobacco consumption, alcohol consumption, and dietary patterns of which tobacco consumption, a common habit in India is foremost. Lung cancer, gastric cancer, oral cancer, colorectal cancer, esophageal cancer, Gall bladder cancer and non-Hodgkin's lymphoma were identified as main cancers attributing to life style factors. Though life style factors like smoking, tobacco consumption, and other oral dip products were common factors in north, south and west India, few risk factors like consumption of salty tea, hookah, sundried foods and red chilly were unique to North India. Cabbage sprouts and Vitamin C rich foods were identified to have protective properties. Consumption of high temperature tea poses a risk of esophageal cancer while coffee has protective tendencies. Also, the consumption of various fruits and vegetables that are rich in vitamins and carotene have anti-oxidant effects which reduce the risk of lifestyle cancers. Among non-vegetarian diets, fresh fish is a protective factor while the risk associated with meat consumption is not yet established. However, the exposure of dry fish to harmful micro-organisms during preservation makes it a threat to the body. Amongst females, cooking methods such as the use of non-liquefied petroleum gas, cow dung, coal and wood and also exposure to passive smoking, high parity, and early pregnancy also emerged as risk factors for life style cancers. Contributory factors like occupational exposure, low education, and low socio-economic status have also been identified with these cancers. There is variation in the incidence of risk factors in different regions due to the diversity of lifestyle patterns in India, a reflection of what exists in the globe. This review therefore implies the need for better and more effective awareness programs which focuses not only on widely known risk factors but also those that are yet to be established. Also, establishment of tobacco and smoking cessation programs at various levels and enactment of policies to strengthen preventive measures are strongly recommended to achieve a decline in the burden of lifestyle cancers.

Limitations of the Study

Due to time constraint, the reviewer could not explore other databases like CINAHL which could have added to the available studies in the reviewed area. In addition, only published data that was available online was used by the reviewer leaving grey literature out of scope of this review.

What is known about the Topic

- Cancer is a leading cause of death globally and consumption

of Tobacco and Alcohol are highly associated with lifestyle cancers.

- In India, 70% to 90% of cancers can be associated to lifestyle and can be easily prevented by adapting healthier lifestyles.

- India has the highest number of oral cancer cases in the world due to the common habit of chewing tobacco in the country.

What the Paper Adds

- In addition to the consumption of Tobacco and Alcohol which is generally associated to lifestyle cancer, dietary pattern, consumption of hookah, salty tea, poor food preservation, occupation hazards and poor socio-economic status were also associated with the incidence of lifestyle cancers in India and were specific to North India.

- Diversity of lifestyle patterns were noted in the different geographical locations in the country and therefore informed variation in the incidence of risk factors of lifestyle cancers in India

- Esophageal, gastric, colorectal, oral, Non-Hodgkin Lymphoma, lung and Gall bladder cancers have been associated with lifestyle risk factors in India.

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