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Incidence and Pattern of Distribution of Cancer in Northeastern Region of India: A Secondary Data Analysis

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Abstract: Cancer is rapidly emerging as a significant public health issue worldwide, including India. In wealthy nations, it is the second major cause of death, while in developing nations, it ranks third. The Northeastern region of India experiences a disproportionately high cancer burden, with elevated occurrence and fatality rates in relation to other parts of country. The main aim of this study is to characterize the cancer incidence in the Northeastern region of India and to understand the gender-specific trends of cancer prevalence in North eastern region. The study aims to characterize cancer incidence and gender-specific trends in the Northeastern region, providing valuable insights for public health interventions and resource allocation. This study used data from 15 Population-Based Cancer Registries (PBCRs) from 2012 to 2016 to evaluate the incidence and geographic distribution of several malignancies in India's Northeast region. The analysis revealed that esophageal cancer was the most prevalent kind among men, followed by stomach and lung cancers. Breast cancer was the main malignancy among women, preceding cervical cancer. Notably, nasopharyngeal cancer, uncommon in other regions, was prevalent in the Northeast. Risk factors such as tobacco consumption, dietary habits, betel nut chewing and alcohol consumption were identified as contributing to these patterns. The findings highlight the importance of targeted public health measures to address these risk factors and enhance early detection, prevention, and treatment of cancer in the region.

Keywords: Cancer, Gender specific trends, Risk factors, Northeast region, Population-based cancer registries

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Introduction

Cancer is becoming the most important public health issue in India as well as around the globe. In developed nations, it ranks as the second major cause of death, while in developing nations, it is the third (Bener *et al.*, 2008). Patterns of cancer

incidence are different in various regions due to eating habits, socio-economic status, cultural attributes, lifestyles and diversity in ancestries (Basu *et al.*, 2016; Shanker *et al.*, 2021). Cancer is the world's second greatest cause of mortality; it

accounts for one in every six fatalities, with 70% occurring in low- and middle-income nations.

India's cancer burden would significantly increase from 979,786 cases in 2010 to 1,148,757 cases in 2020 (Sharma *et al.*, 2004; Ngaihte *et al.*, 2019). In India, mortality due to cancer doubled from 1990 to 2016 (Tomasetti *et al.*, 2017; Albuquerque *et al.*, 2018). Previously, In India, the most prevalent cancers were oral, breast, and cervical. The present report indicates that there is increased incidence of lung cancer as compared to oral and breast cancer. India's cancer landscape mirrors global patterns, with rising lung, breast, and prostate cancers. However, oral, breast, and cervical cancers remain dominant, comprising over half of all cases (Dikshit *et al.*, 2012; Shetty *et al.*, 2020). The National Cancer Control Program focuses on methods of prevention such as promotion of tobacco control, maintenance of genital hygiene, screening for cervical cancer, breast cancer and oropharyngeal cancer etc. (Arora *et al.*, 2009).

In the Northeastern region of India, the rate of mortality due to cancer is continuously increasing. The overall pattern of incidence also differs in the regions of northeast as compared to other part of the country. In terms of mortality and incidence statistics, the majority of the Northeast regions have highest rank for a variety of cancer sites for both sexes (male and female) (Phukan *et al.*, 2006).

Occurrence of different types of cancer in a population is closely associated with various risk factors. It has been demonstrated that risk factors of cancer include smoking, chewing of tobacco, consumption of alcohol and consumption of spicy food etc. (Kataki *et al.*, 2011; Saikia *et al.*, 2023).

The prevalence as well as distribution of malignancies across the country give valuable data for policymakers and advocacy groups to improve cancer prevention and early detection planning (NCRP-ICMR, 2013). Additionally, it can support the proper distribution of resources for cancer research as well as the reporting of cancer patient

data. Since 1982, data on cancer disease have been collected by the National Centre for Disease Informatics and Research (NCDIR) and the Indian Council of Medical Research (ICMR) (NCRP-ICMR, 2014). The National Cancer Registry Program compiled and released cancer data spanning from 2012 to 2016 in 2020, encompassing information from a network of 28 registries nationwide (Mathur *et al.*, 2020).

These registries are classified into two types: Population-based (PBCR) and Hospital-based (HBCR). Population-based cancer registries (PBCR) methodically collect data on incidents of cancer. from diverse sources within a specific geographic region over a year. In contrast, hospital-based cancer registries (HBCRs) focus on patient data related to cure, administration, and outcomes within a specific hospital (Sarkar *et al.*, 2020). Cancer registries capture information on age groups, cancer occurrence, mortality, crude incidence rate, age-specific rates, and standardized rates. The cancer registry report offers a comprehensive overview of cancer incidence, distribution patterns, and overall burden nationwide (NCRP-ICMR, 2014).

The present study focused to highlight the incidence and distribution pattern of various cancer types across eight states and analyzed cancer incidence data to identify which gender are most affected by several cancer types that we have to concentrate on reducing cancer incidence and eventually, the mortality and morbidity caused by the disease in India's northeastern area.

Materials and Methods

General study details

The current study is based on secondary data analysis, including data acquired from the National Cancer Registry Program (NCRP) report in July 2020. The report included the cancer registry data from 2012-2016. For this study we did not receive any institutional ethics committee approval because the data were freely accessible. The patients were not contacted directly, and the study did not contain any patient identities. As a

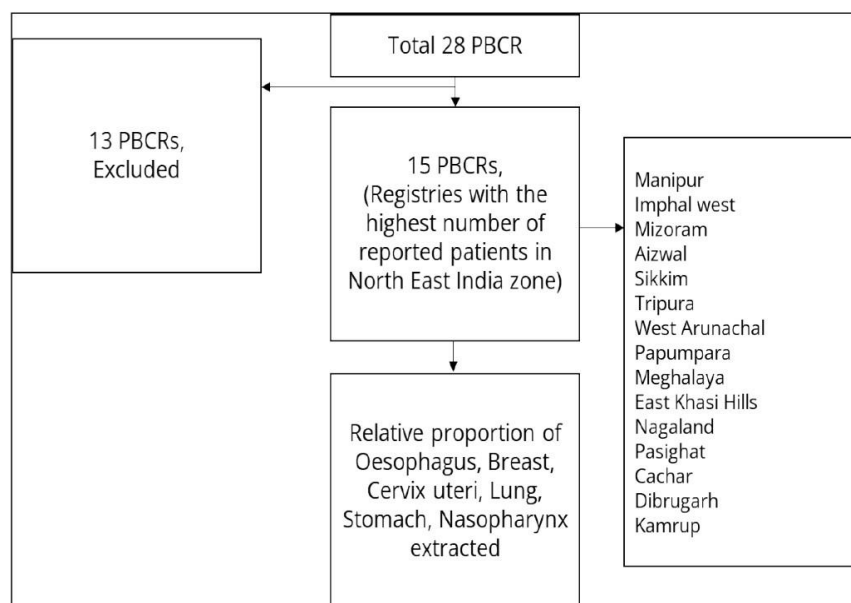


Fig. 1: Flow diagram showing the result based on PBCR.

result, the patient's informed consent was not acquired.

Participants/source of data

The study utilized data from published reports of 28 population-based cancer registries (PBCRs) and 58 hospital-based cancer registries (HBCRs). The Indian Council of Medical Research (ICMR) compiled and released this data, making it publicly available. For this analysis, we exclusively used data from PBCRs, as it was considered more suitable for examining cancer trends on a population level. 15 PBCRs were chosen which are geographically divided into the northeast region of India. From these 15 PBCRs, a total of 79,691 patients has been incorporated into this study as shown in Figure 1.

Variables

The major purpose of this study was to determine the pattern of cancer incidence in North eastern region in India. In addition, we also focused to determine the malignancies which are appearing more frequently and whether the prevalence of other cancers is also rising in northeast India.

Study methodology

The study encompassed Population-Based Cancer Registries (PBCRs) from Manipur, Mizoram, Sikkim, Tripura, Pasighat, Papumpare, Meghalaya, Nagaland, Cachar, Dibrugarh, and Kamrup. Relative proportions of breast, lung, nasopharyngeal, esophageal, stomach, and cervical cancers were calculated for each PBCR. Comparative analysis of these proportions was conducted to identify emerging cancer patterns in the northeast India.

Results

The overview of the PBCRs and the procedure of extraction of their corresponding data are demonstrated in Figure 1. Six PBCRs identified esophageal cancer as the most prevalent among men, while five reported stomach cancer as the leading cancer in this group. Lung and nasopharyngeal cancers followed in frequency. Six PBCRs showed that breast cancer was the most frequent malignancy among women, followed by cervical cancer (Table 1).

The relative proportions of the selected types

Table 1: Leading cancer types for males and females in population-based cancer registries (2012-2016)

PBCR	Gender	Cancer (in specific organ)
Aizawl	Male	Oesophagus
	Female	Lung
Cachar	Male	Oesophagus
	Female	Cervix uteri
Dibrugarh	Male	Oesophagus
	Female	Breast
East Khasi Hill	Male	Oesophagus
	Female	Oesophagus
Imphal	Male	Lung
	Female	Breast
Kamrup	Male	Oesophagus
	Female	Breast
Manipur	Male	Lung
	Female	Breast
Meghalaya	Male	Oesophagus
	Female	Oesophagus
Mizoram	Male	Stomach
	Female	Cervix uteri
Nagaland	Male	Nasopharynx
	Female	Cervix uteri
Papumpare	Male	Oesophagus
	Female	Breast
Pasighat	Male	Stomach
	Female	Cervix uteri
Sikkim	Male	Stomach
	Female	Breast
Tripura	Male	Lung
	Female	Cervix uteri
West Arunachal	Male	Stomach
	Female	Stomach

(Source: Report of National Cancer Registry Program 2012-2016)

of cancer from the selected PBCRs are tabulated in Table 2 and Figures 2 and 3 which show their mean relative proportions (in percentage). Overall, this study result demonstrated that the

mean relative proportion of breast cancer is highest among women, while in men, esophageal cancer shows highest mean relative proportion of cancer across all PBCRs (Table 2).

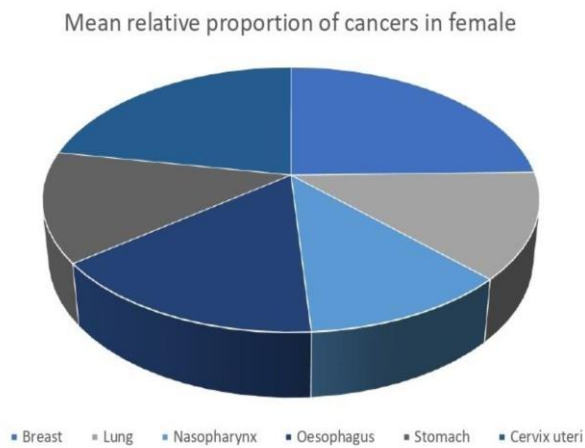
Table 2: Relative proportion of specific cancers in the selected population-based cancer registries (%) in Northeast India (2012-2016)

PBCR	Gender	Breast (%)	Lung (%)	Nasopharynx (%)	Oesophagus (%)	Stomach (%)	Cervix uteri (%)
Manipur	Male		18.9	6.2	5.3	6.9	
	Female	15.4	14.4	2.7		3.5	9.5
Imphal	Male		18.2	3.7	5.5	3.6	
	Female	15.7	14.3				8.5
Mizoram	Male		14.3	2.6	15.4	18	
	Female	13.5	14.1		3.7	10	15.4
Aizawl	Male		13.2		18.3	15.7	
	Female	15.4	16		4.1	9.2	14.8
Sikkim	Male		7.1	5.5	7.8	16.9	
	Female	12.2	6.5		4.6	7.3	10.3
Tripura	Male		16.8		7.7	6.2	
	Female	14.4	5.4		4.9	3.7	16.5
West Arunachal	Male		6.5	4.3	7.7	23.2	
	Female	12.1	3.9		2.8	14.6	11.6
Papum Pare	Male		6.1		31	6.3	
	Female	8	4.1		4	7.2	
Meghalaya	Male		5.3		31	6.3	
	Female	8.2	4		22.3	7.2	8.7
East Khasi Hill	Male				33.7	5.3	
	Female	8			27	7.1	10
Nagaland	Male		6	14.3	10.6	12.6	
	Female	12.2	3.7	9.8		11.3	16.4
Pasighat	Male		7.8		5.6	18.1	
	Female	16.8	3		4	9.6	18.5
Cachar	Male		8.6		11.6	4.2	
	Female	14.1	3.2		7.5	3	15.4
Dibrugarh	Male		5.3		15.7	7.3	
	Female	20.3	2.3		9.1	5.3	6.2
Kamrup	Male		7.9		14.3	6.3	
	Female	17.5	3.8		9.5	4.7	8.6
Mean relative proportion- North east India	Male		10.1	6.1	14.7	10.5	
	Female	13.6	7.1	6.3	8.6	7.4	12.2

Relative proportion: It is the proportion of a specific cancer type in relation to all the other cancer types in a particular cohort or population. *Mean relative proportion:* arithmetic mean of the relative proportions of a specific cancer type in different populations. (Source: Report of National Cancer Registry Program 2012-2016).

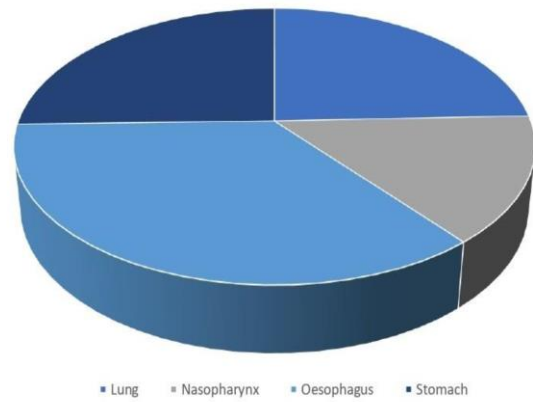
Crude rate (CR), age-adjusted rate (AAR), and truncated rate (TR) per 100,000 populations for all sites of Cancer are illustrated in Table 3. The highest crude rates (CR) per 100,000 populations have been observed in Aizawl district among both

male and female. Papum Pare of Arunachal Pradesh had the highest AAR among females and Aizawl district had highest rate of AAR among females. The truncated rate (TR) per 100,000 populations among male and female have been



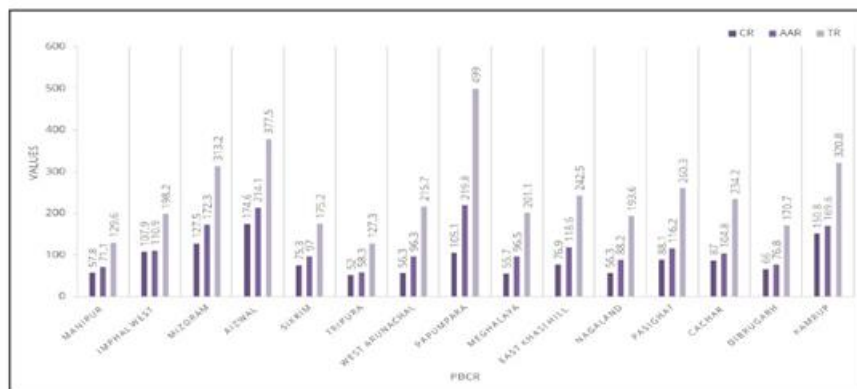
(A)

Mean relative proportions of cancers in male

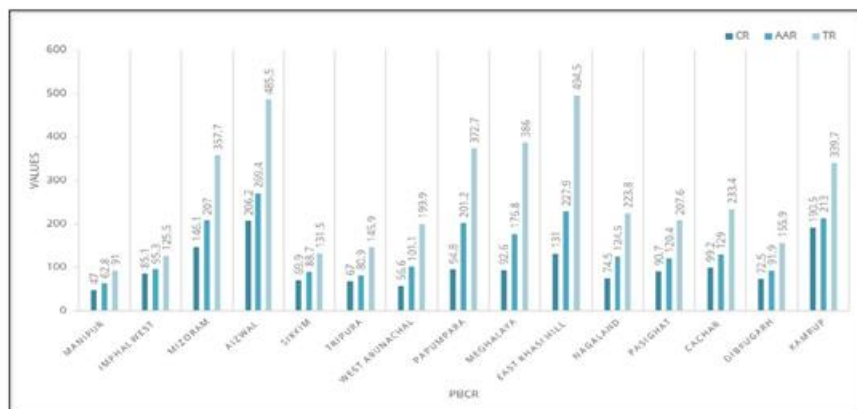


(B)

Fig. 2: (A) Mean relative proportion of cancers (breast, lung, nasopharynx, oesophagus, stomach and cervix uteri) in female; (B) mean relative proportion of cancer (breast, lung, nasopharynx, oesophagus and stomach) in male.



(A)



(B)

Fig. 3: Comparison of AAR (Age-adjusted rate), CR (Crude rate, TR (Truncated rate- 35- 64 years par I lakh population (A) female and (B) male. In different PBCRs of northeast India.

Table 3: Incidence rate - Crude rate (CR), age-adjusted rate (AAR), and truncated rate (TR) per 100,000 populations for all sites of Cancer of population-based cancer registries (PBCR) in northeast region

S. No.	Registry	Males			Females		
		CR	AAR	TR	CR	AAR	TR
1	Manipur State (2012-2016)	47	62.8	91	57.8	71.1	129.6
2	Imphal west (2012-2016)	85.1	95.3	125.5	107.9	110.9	198.2
3	Mizoram (2012-2016)	146.1	207	357.7	127.5	172.3	313.2
4	Aizawl (2012-2016)	206.2	269.4	485.5	174.6	214.1	377.5
5	Sikkim (2012-2016)	69.9	88.7	131.5	75.3	97	175.2
6	Tripura (2012-2016)	67	80.9	145.9	52	58.3	127.3
7	West Arunachal (2012-2016)	56.6	101.1	199.9	56.3	96.3	215.7
8	Papumpare (2012-2016)	94.8	201.2	372.7	105.1	219.8	499
9	Meghalaya (2012-2016)	92.6	176.8	386	55.7	96.5	201.1
10	East Khasi Hill (2012-2016)	131	227.9	494.5	76.9	118.6	242.5
11	Nagaland (2012-2016)	74.5	124.5	223.8	56.3	88.2	193.6
12	Pasighat (2012-2016)	90.7	120.4	207.6	88.1	116.2	260.3
13	Cachar (2012-2016)	99.2	129	233.4	87	104.8	234.2
14	Dibrugarh (2012-2016)	72.5	91.9	155.9	66	76.8	170.7
15	Kamrup (2012-2016)	190.5	213	339.7	150.8	169.6	320.8

CR refers to the rate obtained by division of the total number of cancer cases by the corresponding estimated population (mid-year) and multiplying by 100,000. AAR is calculated according to the direct method (Boyle and Parkin, 1991) by obtaining the age specific rates and applying these rates to the standard population in that age group. (Source: Report of National Cancer Registry Program 2012-2016)

observed in East Khasi Hills and Papum Pare, respectively.

Discussion

In this present study, we have analyzed the 15 PBCRs in which 10 registries represent the data of incidence of esophagus cancer followed by stomach cancer as leading cancer in men. In women it has been found that breast and cervix uteri cancer are the most prevalent cancer site in northeastern part of India.

To assess the emerging type of cancers in northeast India, the relative proportion of nasopharynx, along with lung, stomach cancer were also examined. Table 2 depicts the mean relative proportions of esophagus, lung, stomach and nasopharynx cancers which is 14.7%, 10.5%, 10.1% and 6.1%, respectively in men. The mean relative proportions of the breast, nasopharynx,

lung, oesophagus, stomach, cervix uteri cancers are 13.6%, 6.3%, 7.1%, 8.6%, 7.4%, and 12.2% in women, respectively.

Among males, the five highest crude rates (CR) per 100,000 populations have been noticed in Aizawl (206.2), following that Kamrup urban (190.5), Mizoram (146.1), East Khasi Hill (131) and Cachar (99) (Table 3). Likewise, among females, the five highest crude rate (CR) was noted in Aizawl (174.6) which is followed by Kamrup urban (150.8), Mizoram (127.5), Imphal (107.9) and Papumpare (105.1). A comparison of the Age adjusted rates (AAR) per 100,000 populations of 15 PBCRs represented a high occurrence of cancer in the northeast India. Among all PBCR's Aizawl district have shown highest AAR at 269.4 for men on the other hand for women AAR is highest in Papum Pare of Arunachal Pradesh at 219.8. The

range of truncated rate (TR) per 100,000 population in males is 91 in Manipur to 494.5 in East Khasi Hills which is followed by Aizawl (485.5). Likewise, TR ranged from 127.3 in Tripura to 499.0 in Papum Pare district of Arunachal Pradesh in females.

The trends of incidence of cancer in the northeastern region is somewhat different from the other parts of the country. Nasopharynx cancers, which are rare in other regions of India, but are prevalent in northeast region. Various studies show the association of nasopharynx cancer with the Infection of Epstein-Barr virus (EBV) in northeast India (Lourembam *et al.*, 2015). Some important risk factors include lack of fruit intake, living in houses which are poorly ventilated and ingestion of nitrosamine-containing food items (Sharma, 2011).

The limitations of this study is that it could not be performed a comprehensive data analysis because the total numbers were not accessible. Therefore, it may not be proper demonstration of the ground reality.

Risk factors of various cancer types

There are various types of factors which contribute to the incidence of different types of cancer in these regions. Thapa *et al.* (2013) identified several potential risk factors contributing to elevated breast cancer incidence rates. These factors include higher educational attainment, occupational stress, delayed menopause, induced abortion history, first-degree family history of the disease, and body mass index (Fortner *et al.*, 2016). Risk factors for breast cancer include alternations of 2 sequences and BRCA1 (Saxena *et al.*, 2016). Numerous studies have linked female sex hormones to breast cancer development. Early menarche (before age 12) doubles the breast cancer risk compared to later onset. Additionally, women experiencing menopause after age 55 have a 22% higher relative risk than those reaching menopause before age 45. Breastfeeding has been linked with a slight limiting in breast cancer risk (Aich *et al.*,

2016).

Esophageal and stomach cancers are the other most prevalent cancers among men. The high incidence of these cancers is likely linked to tobacco consumption, including smoking and the use of smokeless forms like chewing tobacco and tuibur. Additionally, dietary factors such as excessive consumption of smoked, cured, or fermented foods, including meat, vegetables, and soybeans, may also contribute to the risk (Mahanta *et al.*, 1998; Ghatak *et al.*, 2016). Betel nut chewing in regions like Assam, is the prime risk factor for esophageal cancer (Russo *et al.*, 2001). The dietary habits prevalent in India's northeastern states are associated with increased cancer risk. Practices such as smoke-drying, lead to the formation of N-nitroso compounds, known carcinogens. These compounds arise from the interaction of nitrites with proteins (Chetia *et al.*, 1996; Chatterjee *et al.*, 1999). While salt itself is not carcinogenic, excessive consumption can damage the stomach lining, increasing the risk of gastric cancer. This damage can progress to chronic inflammation and ultimately, cancer. The combined presence of salt and nitrites in processed fish and meat exacerbates this risk (Phukan *et al.*, 2001; Phukan *et al.*, 2006). Frequent consumption of "sa-um," a fermented pork fat unique to Mizoram, has been connected to an increased risk of stomach cancer. High dietary intake of total or saturated fat is also associated with this disease (Lopez *et al.*, 1999). Boiled pork fat, rich in saturated fat, can potentially form carcinogenic compounds during prolonged storage (Malkin *et al.*, 1997; Chen *et al.*, 2002; Navarro *et al.*, 2008). Soda, commonly used as a food additive in Northeastern India, has been identified as a risk factor. The high methylation activity in salted cooked vegetables prepared with sodium bicarbonate can lead to the formation of nitrosamines, which are linked to stomach cancer (Verma *et al.*, 2012; Misra *et al.*, 2013). A study done in Sikkim shows the prevalence of a co-carcinogen *Helicobacter pylori* infection in this area (Hammond, 1996).

Tobacco use is the primary cause of cancer in northeast India. Smoking, chewing, and other forms of tobacco consumption account for a substantial portion of cancer cases, ranging from 65% to 85% in men and women, respectively. These harmful habits are linked to cancers of the mouth, pharynx, esophagus, larynx, lungs, and bladder (IARC, 2023). Smoking, in particular, is strongly associated with lung cancer (Jayant *et al.*, 1991). Tobacco smoking, particularly through bidis and cigarettes, is responsible for approximately 87% and 85% of lung cancer cases in Indian men and women, respectively (Bano *et al.*, 2009). Studies by Jussawalla and Jain (1979) and Pakhale *et al.* (1990) have confirmed the highly carcinogenic nature of locally produced Asian cigarettes. The unrefined tobacco in bidis and the higher frequency of puffs compared to cigarettes contribute to their greater carcinogenic potential. In fact, two puffs of a bidi release similar levels of harmful substances, such as steam volatile phenols, hydrogen cyanide, and benzopyrene, as one puff of an unfiltered cigarette (Pakhale *et al.*, 1990). Additionally, hookah smoking has been linked to lung cancer (Nafae *et al.*, 1973).

Areca nut, pan masala, opium, and bhang consumption are primary etiological factors for oral cancer. Chronic exposure to betel leaf, commonly consumed at rates of 15-25 leaves daily in certain northeastern states, induces chronic irritation of the buccal mucosa (Mehrotra *et al.*, 2003). Raw betel nut chewing is a critical risk factor for oropharyngeal malignancy. Betel quid chewing is associated with a relative risk of 1.5 to 3.5 for esophageal cancer development (Wahi *et al.*, 1965).

The link between alcohol consumption and an elevated risk of esophageal cancer was established as early as 1910 (Tuyns, 1979). Chronic alcohol use has been linked to upper respiratory and digestive tracts cancer, including the oral cavity, liver, larynx, pharynx, esophagus, pancreas, breast, and mouth (Murthy *et al.*, 2004). Women consuming 10 g of alcohol daily exhibit a 7.1%

increased relative risk of breast cancer. While the exact mechanism of alcohol-induced carcinogenesis remains unclear, ethanol is believed to act as a co-carcinogen, playing a crucial role in cancer development. Ethanol metabolism generates acetaldehyde and free radicals, which contribute to carcinogenesis by damaging DNA and proteins, leading to abnormal cell growth (Doll *et al.*, 1981).

Non-tobacco risk factors for cancer encompass a range of factors including infections, dietary habits, alcohol consumption, physical activity levels, body composition, exposure to asbestos, air pollution, occupational hazards, and radiation (Irigaray *et al.*, 2007; Anand *et al.*, 2007). Alcohol consumption is connected with elevated risk for cancers of pharynx, oral cavity, colon, larynx, breast, rectum, and esophagus. Aflatoxins, arsenic, and beta-carotene supplements have been identified as risk factors for liver and lung cancers, respectively (Tuyns, 1979; Maier *et al.*, 1994; Seitz *et al.*, 2004). Excessive consumption of red and processed meat is linked to colorectal cancer. Additionally, infections such as HPV, hepatitis C virus, 'Kaposi sarcoma-associated herpesvirus and Epstein-Barr virus have been implicated in specific cancer types (Harford, 2012; Anil *et al.*, 2014; Tomasetti *et al.*, 2017).

Conclusion

In this secondary data analysis, we have studied that the proportion of cancer is still high in the northeastern region of India. Most cancers in the northeast India are different from other part of the country. In the men oesophagus and stomach cancer are more prevalent while in women breast and cervix uteri cancer are very common. On the basis of PBCRs the Mizoram state presented the highest number of cancer patients, therefore it could be known as the red zone for cancer incidence. Our secondary data analysis provides variable data over a period of 4-year which could be applied not only to recognize the etiology and epidemiology related with different cancers which also help for designing cancer control programs and treatment facilities in this region.

Ethical Statement

For this study there is no need of any institutional ethics committee approval because the data were freely accessible. The patients were not contacted directly, and the study did not contain any patient identities. As a result, the patient's informed consent was not acquired.

Author Contributions

All authors have read and agreed to the published version of the manuscript.

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Conflict of Interest

The authors declare no conflicts of interest.

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