Patterns of Cancer Incidence and Mortality in North- Eastern India: The First Report from the Population Based Cancer Registry of Tripura

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Abstract

**Background:** There is, till date no population-based data regarding cancer patterns in North- Eastern India, dictating the need to understand the epidemiology of cancer in this population for its effective management. **Methods:** This is the first report of the Population Based Cancer Registry (PBCR) in Tripura (2010-2014). The protocol involves active collection of data on all cancer cases from Tripura through staff visit in more than 150 sources of incident and mortality registration, government and private hospitals, municipal corporation, etc. and scrutiny, corroboration with existing records. Data was analyzed statistically to understand cancer trends in terms of incidence and mortality across different sites, age groups affected and gender. **Results:** A total of 10,251 cases were registered during the period, with overall age-adjusted incidence rates of 75.7 and 54.9 per 100,000 males and females respectively. Crude Incidence Rate (CR) and Age- Adjusted Rate (AAR) was among the lowest reported in India, probably due to associated socio-economic factors. The most prevalent cancers were lung (18.1%), esophageal (8.3%) for men and cervix uteri (17.6%), breast (13.8%) for females. Gall bladder cancer in females was one of the highest in the country. Rate of cancer mortality in the population was quite high and significantly increased with time, probably accounting for dearth in early detection and feasible treatment alternatives. **Conclusion:** The data suggests that high cancer incidence and mortality are prevalent in the population of Tripura, dictating the need of active tobacco control measures, early detection and awareness drives for effective cancer control.

**Keywords:** Cancer registration- control- prevention- epidemiology- North- Eastern India

Introduction

The National Cancer Registry Programme (NCRP) was introduced by Indian Council of Medical Research (ICMR) in 1981 and currently holds a network of 28 Cancer Registries across the country. However, initiatives taken in North- Eastern India is relatively recent, leading to lack of reliable population- based cancer data from this part of the country. According to the latest census in India in 2011, the Indian population has already crossed 1.2 billion and not only comprises of an immense versatility in ethnicity, culture, language and other socio- economic parameters, but also in terms of distribution and patterns of both chronic and infectious diseases.

The Cancer Atlas Project was established in 2006 by NCRP, which was subsequently recognised as a Population Based Cancer Registry (PBCR) in 2009 at the prestigious Regional Cancer Centre (RCC), Agartala, to cater to cancer data collection from the entire state of Tripura. PBCR specifically focus on the cancer disease burden in terms of incidence and survival in a population residing in a specific geographic area and use of the data for evaluation and planning of disease management (Jensen et al., 1991).

The state of Tripura is located in the north- eastern part of the country between the latitudes 22056’, 24032’ (North) and longitudes 91009’, 92020’ (East). The altitude at the capital of Tripura, Agartala, is 12.80 m. Tripura has a strategic location in that it shares about 84% of the total perimeter of international border with Bangladesh. Although relatively small in terms of size (10,491.69 sq.km), 60% of the area is hilly and forested 27% is cultivated. The population is over 3.5 million with 960 females per 1000 males and has a high overall literacy rate of 87.2 %. The population is multi- religious, although predominantly Hindus (85.6 %) and multi- lingual, although...
the most common language is Bengali. Interestingly, 
Tripura houses diverse ethno-linguistic tribal groups 
with Bengali culture co-existing with Tribal traditional 
practices.

Till date, there are very few reports regarding the 
cancer scenario in different parts in India and to the 
best of our knowledge, no comprehensive reports from 
the north- eastern part of the country. Data on cancer 
incidence and mortality were collected for a 5-year period 
from 2010-2014 to understand the trends in this part of 
the country. Our observations indicate that cancer incidence 
and mortality was quite high in Tripura, although 
the overall 5-year trend of all cancers remained similar, 
dictating the need for effective tobacco regulation, cancer 
screening and control in this part of the country and in 
India in general.

Materials and Methods

Sources of registration

Cancer is not yet a notifiable disease in India and 
hence, registration is not voluntary. Thus, data was 
collected through active participation of social workers 
through visits to different sources and by interviewing 
patients/attendants and scrutinizing medical records. 
The main registration source for cancer patients of Population 
Based Cancer Registry, Tripura, is the Regional Cancer 
Centre, Agartala (86.6-97.1% cases from 2010-2014), 
due to its being the lone State hospital of cancer treatment 
in Tripura where the PBCR is also located. There are 
however more than 150 sources for Incident, Mortality 
registration in the whole state including Government 
hospitals (121), private hospitals (1), nursing homes 
and polyclinics (12), private pathological laboratories 
and radiological centres (25), Death, Birth Registry, 
Municipal Corporation, Crematory, Village Panchayet, 
etc. Majority of the mortality data was obtained from 
social investigators during their home visit activities apart 
from their normal visits of hospitals, crematory, death, 
birth registry office etc. A total of 10,251 incident cancer 
cases were registered during the period from 2010 to 2014. 
Clearance from the institutional ethical committee was 
obtained prior to the study, as well as written informed 
consent from all participants.

Parameters for collection of data

Primary site and histology were categorised according 
to International Classification of Diseases for Oncology 
(ICD) (Jensen et al., 1991). All clinic-pathological and 
demographic data were manually and electronically 
recorded, including identifying information of the patient, 
residential address, duration of stay at permanent address, 
date of first diagnosis, diagnosis status, ICD coding, etc. 
Informed consent was obtained from all the patients 
prior to the study. The data was then matched with the 
incident database of RCC, Agartala and PBCR. Data 
on mortality was collected from previously mentioned 
sources to include details and matching of mortality 
data with morbidity cases was carried out (Fritz et al., 
2013). Non-matched death cases and those with no case 
history, other than the availability of death certificate were 
registered as “Death Certificate Only” (DCO) and entered 
into the database along with ICD coding (flow chart in 
Supplementary Figure 1, Supplementary Table 1). All 
new data were thoroughly verified with those existing in 
the registry to avoid duplication.

The registry is reported in the span of five years from 
2010-2014 and reported in terms of sex, site, Crude 
Incidence rates (CR), Age-Adjusted Incidence Rates 
(AAR) and Truncated Rate (TR) per 100,000 persons and 
directly using world standard population (Sen et al., 2002).

Statistical analysis

Chi square for trend (Extended Mantel Haenszel) was 
used to detect the linear variation with subsequent time 
and p value was used to understand significance (Sarkar 
et al., 2017). All tests were two tailed, with a Confidence 
Interval (CI) of 95% and probability (p) value <0.05 being 
considered significant. Calculations were by softwares Epi 
Info 7 (CDC, Atlanta).

Results

Males presented with higher pre-disposition to risk and incidence the disease

According to the 2011 census, the population of 
Tripura was 36,73,917, out of which there were 18, 
74,376 males. A total of 10,251 cases were registered 
during the 5-year period from 2010-2014, out of which 
there were 5,859 males and 4,392 females (Table 1). 
The number of patients progressively increased over 
time. Males presented a higher population at risk and 
incidence to malignancy (Table 1). Among the reported 
malignant cases, males presented with higher CR than 
females (61.4, 47.9 respectively) (Figure 1A). Similarly, 
in AAR and TR, males present with a higher fraction 
(75.7, 136.1 respectively) compared to females (54.9, 
120.2 respectively) (Figure 1A).

Patients presented with a relatively older age of onset, although 5-year disease burden remained similar

Due to lack of estimated distribution of the population by 5-year age group during the census report of 2011, 
the data was obtained from Indian Council for Medical 
Research (ICMR) for the period 2010-2014 (Figure 
1B). Age group 35-64, which represents about 25% of 
the population carried the maximum incidence of new 
malignant cases, about 60%, indicating the significant 
positive correlation of cancer with the biological process 
of ageing (p for trend from ages 0-64 years <0.001) (Figure 
1C). The population having lower age group was greater 
but had lower disease burden. Interestingly, the incident 
rate of cancer at the older age group (>35 years) was 
high despite the lower percentage of individuals within 
that age window, indicating the correlation of cancer 
with increasing age (Figure 1C). The trend in cancer 
burden in a 10-year age group distribution remained 
similar in both males and females (Figure 1D, E, Table 2). 
However, differential pattern in age-related distribution 
was observed between both genders, with older men and 
middle-aged women presenting a higher propensity to 
develop cancers (Figure 1D, E).
Specific cancers presented at a higher incidence rate but with comparable annual 5-year trends

The incidence of a particular cancer was similar in the time span studied (Figure 2A). Lung and esophageal cancers were the highest among men (5-year average 18.1%, 8.3% respectively), while cervical and breast cancers were the highest among women (5-year average 17.6%, 13.8% respectively) (Figure 3A), probably due to associated lifestyle and risk factors. Within the time frame studied, tobacco-related cancers were quite high among both men and women with differential distribution of the various sites affected (Figure 2B). Lung and esophageal cancer were the highest among men (18.1%, 8.3% among tobacco-related cancers), while esophageal and lung were the highest among women (5.4%, 4.5% respectively).

High rate of mortality was observed in the population

Cancer-related deaths among males and females was high in Tripura and in the ratio of 8:5. Deaths due to cancer was 8.2% among all deaths. Overall mortality per incidence increased with progressing years (Figure 3A). The mortality versus incidence of cancer was higher in males, as was CR and AAR (Figure 3B, C). The incidence of mortality ratio in different cancers varied with cancer
types in increasing ratios annually (Figure 4D). Among men, highest mortality was due to lung and liver cancers (5-year average M/I 61.3, 59.7 respectively), while those among women were due to stomach and gall bladder cancers (5-year average M/I 59.6, 54.8 respectively). Most cancers presented a significant rise in mortality in the 5-year period studied (Figure 3D).

Discussion

Knowledge on the trends in different cancers are essential for designing strategies for effective cancer control globally. Although cancer prognosis in terms of death and years of life lost provide valuable information, data regarding cancer incidents in the population provide valuable information to understand the risks and risk factors associated with various cancers, which in turn aids in early detection and prevention.

In-depth analysis of the 5-year data of the Tripura Population-Based Cancer Registry provides an invaluable insight into the cancer patterns in this north-eastern state of India, with its unique ethnic and socio-economic setting. The data has been reported two years after promotion of the National Cancer Registry Program (established, 2006) into the Population-based one, hence eliminating most factors of under-reporting. However, those cases which were at all missed were probably in advanced cancers with dismal prognosis, especially in older patients diagnosed in outpatient clinics. These patients might not have received any curative treatment, thus eliminating medical records and hence registration. However, the authors believe that most of these cases would be efficiently recorded through DCO.

The CR and AAR, as well as TR in males and females

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Table 1. Population at Risk (Males and Females) in Tripura and the Malignant Cases Diagnosed between the Years 2010-2014

| Year | Population at Risk | Number of Malignant Cases |
|------|---------------------|--------------------------|
|      | Males | Females | Total | Ratio (M:F) | Males | Females | Total | Ratio (M:F) |
| 2010 | 1,857,926 | 1,782,253 | 3,640,179 | 10:09 | 1,139 | 846 | 1,985 | 13:10 |
| 2011 | 1,882,656 | 1,808,246 | 3,690,902 | 10:09 | 1,092 | 844 | 1,936 | 13:10 |
| 2012 | 1,907,714 | 1,834,618 | 3,742,332 | 10:09 | 1,177 | 866 | 2,043 | 14:10 |
| 2013 | 1,933,106 | 1,861,372 | 3,794,478 | 10:09 | 1,243 | 942 | 2,185 | 13:10 |
| 2014 | 1,958,835 | 1,888,522 | 3,847,357 | 10:09 | 1,208 | 894 | 2,102 | 14:10 |

\( p \) value

0.86

0.84

M, Male; F, Female
increased with time, although the rates were quite low as compared to those obtained in other Indian registries from the period of 2012-2014 (Males, CR range 39.9 (Barshi expanded, 2012) – 160.7 (Thiruvananthapuram District, 2012-2014). The reason might be due to a combination of several factors: 1) low-risk lifestyle of the people in Tripura, including environmental and socio-economic parameters, 2) incomplete and inaccurate reporting of the number of patients diagnosed and treated outside the state, 3) death of patients before diagnosis and, 4) patients unwilling of confirmation of the malignancy due to socio-economic reasons. However, males show an increased incidence rate compared to women, probably accounting for associated etiological factors such as usage of tobacco, alcohol, occupational exposure, etc. (Sinha et al., 2003; Das et al., 2015).

The overall 5-year age group disease burden remained similar in Tripura, the trend being similar to that observed in other cities according to the PBRC report, 2012-2014. Interestingly, although about 25% of the population belong to the age group of 35-64 years, the maximum incidents of cancer, i.e., 63% occur in this group, indicating a significant association between ageing and cancer. Similar results have been previously shown in other studies (SEARO, 2004; Sharma and Radhakrishnan, 2011; Mallath et al., 2014; Thakkar et al., 2014).

The incidence rate varied between different cancers and between males and females, the results being similar with that obtained in other Population Based Cancer Registries. Lung and esophageal cancers were the highest among men, primarily due to habits such as smoking and chewing tobacco, alcohol consumption, etc (Domper Arnal et al., 2015; Malhotra et al., 2016). Similar high incidence of lung cancer has also been reported in other parts of the country and globally (Islami et al., 2015; Malik and Raina, 2015; Noronha et al., 2016). In women, cervix uteri and breast cancers presented the maximum disease burden, being associated factors such as infection with Human Papillomavirus (HPV), poor hygiene and awareness, diet and exercise, genetics, etc. (Hankinson et al., 2004; Haverkos, 2005; Crosbie et al., 2013) In recent studies, high risk HPV has also been associated with the pathogenesis of breast carcinoma (Lawson et al., 2015). High incidence of cervical cancer has similarly been reported in many studies across India (Kaarthigeyan, 2010; Sreedevi et al., 2015). Surprisingly, gall bladder cancer in females (9%) is present at a percentage higher than reported in most parts of the country (PBCR Report, 2012-2014), only comparable to Cachar District (10.3%), Dibrugarh District (10.7%), Kamrup Urban District (9.3%).

Tobacco usage, both in smoking and smokeless forms is linked to a variety of cancers (Kuper et al., 2002; Vineis et al., 2004). Widespread usage of different forms of tobacco, both in men and women (mostly in smokeless form) (Mishra et al., 2015; Nair et al., 2015) accounts for the high prevalence of tobacco associated cancers observed in our study. Several reports, both within Tripura and other parts of India and across different age groups indicate the widespread use of tobacco in our country (Rani et al., 2003; Sinha et al., 2003; SEARO, 2004; Pal and Tsering, 2009; Agrawal et al., 2013; Das and Baidya, 2014; Mishra et al., 2016). Although several Indian legislations for control of tobacco usage exist in India, such as the National Tobacco Control Programme and Tobacco Cessation Services, further stringent regulation needs to be enforced to minimize tobacco associated health hazards (Shimkhada and Peabody, 2003; Mishra et al., 2015).
et al., 2012).

Mortality rate reported in our study was quite high among cancer patients (Overall 5-year M/I= 45.2% for males, 38.2 for females) and showed an increasing trend with time. This rate was much higher than those reported my most PBCRs across the country (M/I % for Males: Range 10.1(Delhi)- 68.9 (Barshi Rural), Females: Range 8.0 (Delhi)- 66.3 (Barshi Rural) and showed a significant increment with time in most types of cancers. The ratio of male to female deaths was 8:5. Lung cancer, which was the most prevalent form of cancer in men was also the leading cause of cancer-related mortality, while stomach cancer ranked the highest among mortality in women. A combination of several factors could account for this high mortality rate- lack of optimal treatment facilities in rural regions, financial constraints of less affluent individuals, lack of screening programs, late stage diagnosis, etc. (Mallath et al., 2014; Tripathi et al., 2014; Gupta et al., 2015). Similar mortality reports on developing countries were reported both in India and globally with data indicating a rise in cancer associated mortality rates in the future (Jemal et al., 2011; Dikshit et al., 2012).

In conclusion, the Tripura Population Based Cancer Registry, despite having certain limitations in terms of quality of data, due to its being in its early stages, provides comprehensive information on the patterns of cancer in the north-eastern part of India. These observations, which provide valuable information over a 5-year period could be used not only to understand the epidemiology and etiology associated with various cancers, but also aid in effective cancer control in this region. Legislatures and awareness programs to control tobacco usage could reduce the disease burden of several tobacco-associated cancers. Early detection, along with a healthy lifestyle, vaccination programs, physical examination and health education should be encouraged in women for control of cervical and breast cancers. These results could act as a useful guide for designing and implementation of cancer control programs and treatment facilities in this region.

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Author Contribution
1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data: SS, DD, SD, SSM, GM
2) drafting the article or revising it critically for important intellectual content: SS, GM
3) final approval of the version to be published: SS, DD, SD, SSM, GM

Conflict of interest
None declared.

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