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Prevalence of Cancer in India with Respect to Leukaemia and their Factorial Relations

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ABSTRACT

Cancer is a growing burden on the healthcare system. Leukaemia is one such commonly reported cancer. In the United States, leukaemia is thought to account for roughly 3.5 percent of all cancer cases and 4 percent of cancer-related deaths. The present article examines the responsible factors for leukaemia cases in India. For the study, trends of cancer incidence (new cases per year), death, and DALYs (Disability-adjusted life years) attributable to all cancers combined and distinct kinds of malignancies. DALYs were selected as the primary measure for disease burden because it accounts for both death and morbidity and is recommended by India's National Health Policy for illness monitoring. The preserved blood samples of prior knowledge of cases were taken for study and analysis. The article highlights the total burden of all cancers in terms of DALYs from 1990 to 2020, followed by incidence and fatalities. Patterns of 10 cancer types that account for the majority of cancer-related and leukaemia DALYs important disparities in cancer distribution between men and females in India have been discussed in the paper. Six more cancer types that are in the top ten most common incident cancers in Indian women and men but are not among the top ten cancers generating the most DALYs are also reported from the study. The age-standardised incidence rate of the major kinds of malignancies like leukaemia showed significant inter-state variability, ranging from 3.3 to 11.6 times for the four most common malignancies (lip and oral, breast, lung, and stomach). Leukaemia CML mortality has been steadily declining over the last 20 years, but AML fatalities have been steadily increasing. In conclusion, total cancer incidence did not rise as quickly as previously anticipated among aging Americans; nonetheless, myeloid leukaemia and Chronic Lymphocytic Leukaemia (CLL) rates dramatically surpassed those of other malignancies. In this paper, we have given a brief overview of the factors responsible for leukaemia and compared to other cancer cases in India, and a major portion is waited for future research.

Keywords: Cancers; Leukaemia; Chronic lymphocytic leukaemia (CLL); Chronic myelogenous leukaemia (CML)

1. INTRODUCTION

Today, cancer is the second biggest cause of mortality worldwide after cardiovascular illnesses[1]. The pandemic of the coronavirus disease 2019 (COVID-19) impeded cancer detection and therapy in 2020-21. Reduced healthcare access due to facility Factors, such as delays in diagnosis and treatment, may temporarily lower cancer and leukaemia incidence but raise advanced stage sickness and mortality. Low cancer awareness, late leukaemia diagnosis, and unequal access to inexpensive curative therapies give cancer patients in low- and middle-income countries like India a worse prognosis than those in high-income countries[2,3]. India's 13.3 billion people live in 29 states and seven union territories, several of which are countries, with varying levels of development, population genetics, environments, and lifestyles, resulting in a heterogeneous distribution of leukaemia disease burden and health loss[4] The general factors include gender, age, blood disorders, family history, congenital syndromes, lifestyle like smoking, high-energy radiation, pesticides or industrial chemicals exposures, and certain forms of chemotherapy and radiation treatment used to treat other malignancies are considered Leukaemia risk factors[3].

An organised and thorough comprehension of the scope and temporal patterns of all malignancies in every state is absent, despite efforts to characterise the cancer burden and epidemiology on a national level in different regions of India and regions of significance for cancer control[6–20] Since healthcare delivery in India is state-based, this information is crucial for cancer reduction action that meets state needs.

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The global burden of leukaemia diseases, injuries, and risk factors study collaborated with the India state level illness burden initiative to develop India's subnational illness burden estimates.

Based on data conducted as part of GBD 2017[8, 21], this project recently published the variable health transition across Indian states from 1990 to 2020. In 2020, as per the scientific prediction, 10,500 children (newborn to 14) and 5090 teenagers (ages 15-19) would be diagnosed with cancer with 1190 and 590 dying from the illness, respectively. Because benign and borderline malignant brain tumours were not mandated to be reported to cancer registries until 2004, our estimates neglect them in favour of 15 years of historical incidence data. The most frequent juvenile cancer is Leukaemia, which accounts for 28 % of cases, followed by brain and other nervous system cancers (27 %), of which more than a quarter are benign/borderline malignant. From 1990 to 2020, we have explained the comprehensive trends in the incidence and health loss caused by each kind of cancer or leukaemia in each Indian state.

Leukaemia occurs when leukocytes' DNA mutates, causing them to lose growth and division control. These altered cells can sometimes bypass the immune system and multiply, displacing healthy cells. AML, CML, ALL, and CLL are the four main subtypes of leukaemia based on the predominant cell type (myeloid or lymphoid) and disease progression rate (acute or chronic). leukaemia prevalence has stayed mostly steady worldwide, however, ethnicity, environmental factors, and life choices have caused regional differences. The cause of leukaemia is uncertain, but radiation exposure is a risk factor.

The article aims to provide a detailed estimate of incidence, prevalence, mortality, and DALYs for 28 kinds of malignancies in every state of India for 31 years from 1990 to 2020. This study was part of the Global Burden of Diseases (GBD), Injuries, and Risk Factors Study 2020 which looked at all causes of illness burden, and also used data from all available sources to do so. While the age-standardised incidence rate of all cancers evaluated collectively has not changed much in India during the last 31 years, the share of the overall disease Cancer-related burden has increased by 100 %, as shown in this study. This research highlights the significant variation in the incidence, mortality, and DALYs of various cancers among Indian states, as well as the fact that tobacco smoking is India's leading contributor to cancer burden.

2. MATERIAL AND METHODS

2.1 Literature Research

Using PUBMED and SCOPUS, we searched for terms such as "burden," "cancer," "leukaemia," "cause of death," "death," "DALY," "epidemiology," "incidence," "India," "morbidity," "mortality," "neoplasm," "prevalence," and "trends," without limitations on language or publication date. We discovered a wealth of useful information on the distribution of cancer in India and its many states, but no papers that thoroughly characterised incidence, prevalence, mortality, and DALYs for all cancer and leukaemia kinds in all Indian states throughout the time.

2.2 Sampling

Preserved and frozen blood samples with prior knowledge of the case were collected for screening, confirmation, and identification of molecular factors.

2.3 Complete Blood Counting (CBC)

The preserved samples were examined using the Beckman Coulter machine which gives us Complete Blood Count (CBC) with Total Leukocyte count (TLC) and Differential Leukocyte Count (DLC).

2.4 Leishman Staining

Slides were prepared with blood samples, and air dried. The slides were treated with Leishman stain for 2 min diluted with buffer solution and incubated for 10 min. Slides were washed and air dried, and observed through a microscope.

2.5 Flow Cytometer

CD markers like CD^4 and CD^8 and other leukaemia CD markers were used to confirm the type of blood cancer. Samples were prepared with the help of marker's dye solution which was used to differentiate the CD markers. The sample was prepared by adding the CD marker's antibodies. Samples were tested and results were evaluated with a graph and final analysis from the machine's printout.

If samples came positive in the immunophenotyping test then it was further processed to identify the types and stages of Blood cancer by using molecular studies.

2.6 Preparing the Lysate

Lysate was prepared from a 1 ml serum sample. 730 µl of Lysis Mixture was added to the test serum and incubated at room temperature for 20 minutes to lyse the sample.

2.7 Flow Cytometer

DNA was bound using Charge Switch Magnetic Beads. The Charge Switch Magnetic Beads were fully resuspended and uniformly distributed in the storage buffer by vortexing tubes. After digesting the sample, 250 µl of ChargeSwitch Purification Buffer (N7) was added. The mixture was incubated at room temperature for 2 minutes to bind DNA to Charge Switch Magnetic Beads. The sample was in the MagnaRack for 3 minutes until the beads formed a compact pellet. Discard the supernatant. The steps were followed to wash DNA.

2.8 Washing of DNA

Supernatant from the MagnaRack tube with pelleted magnetic beads was properly removed. 1 ml of Charge Switch Wash Buffer was added to the tube and pipetted. The pellet formed was removed carefully.

2.9 Elution of DNA

50 µl of Charge Switch Elution Buffer was added to the tube pipetted and incubated at room temperature for 2 minutes. The pellet formed was used for Gene express identification by using q-PCR To determine whether molecular detection and monitoring of CML is comparable using Peripheral Blood (PB) and Bone Marrow (BM) aspirate.

3. RESULTS

In 2016, the overall number of cancer-related DALYs was 50.0 % (95 % UI 46.6-55 %) and the number of cancer-related deaths was 83.3 % (7.9-8.6) in India. These figures represent increases of 90.9 % and 112.8 %, respectively, since 1990. Although there was no discernible change in the age-standardised cancer DALY rate from 1990 to 2020, the crude cancer DALY rate in India increased by 253 percent, ranging from 168 to 342 [22]. There was a 2.6-fold difference in the age-standardised death-associated DALY rate for cancer and leukaemia among the Indian states in 2016. In 2016, the states with the highest crude cancer DALY rates were Mizoram, Kerala, Assam, Haryana, and Meghalaya. The northeastern states of Assam, Mizoram, Meghalaya, and Arunachal Pradesh had the highest age-standardised rates.

In India, the projected number of cancer cases grew from 548,000 in 1990 (95 % UI 520 000–576 000) to 1 069 000 (1 043 000–1 101 000) in 2016. The crude cancer incidence rate in India grew by 282 % (95 % UI 199–355) from 634 % per 100,000 in 1990 to 812 % per 100,000 in 2016, although the age-standardised incidence rate remained unchanged. Kerala and Mizoram had the highest rates of crude cancer and leukaemia incidence, followed by Haryana, Delhi, Karnataka, Goa, Himachal Pradesh, Uttarakhand, and Assam. Mizoram, Meghalaya, Arunachal Pradesh, and Assam, as well as Delhi and Haryana, had the highest age-standardised incidence rates. From 1990 to 2020, the crude cancer incidence rate grew significantly in all ETL state categories, with the largest rise in the high ETL group.

3.1 Leukaemia

The number of leukaemia and all malignancy cases and deaths was tracked. We used American Cancer Society cancer statistics to examine leukaemia and all malignancies cases and deaths in the US from 1998 to 2018. All malignancies climbed 41 % from 1,228,600 in 1998 to 1,735,350 in 2018. The number of cancer deaths grew significantly from 564,800 in 1998 to 609,640 in 2018 (Fig. 1). Leukaemia rates have been rising far faster than other malignancies, from 28,700 cases in 1998 to 60,300 cases in 2018, a rise of 110 percent, with a sharp surge between 2006 and 2007. Leukaemia fatalities, like other cancer fatalities, rose marginally from 21,600 cases in 1998 to 24,370 cases in 2018. CML, AML, CLL, and ALL, the four primary subtypes of leukaemia, exhibited unique distributions of incident cases and fatalities, with CLL and AML growing quickly in both numbers and percentages. CLL cases climbed drastically from 7,300 in 1998 to 20,940 in 2018, an increase of 187 percent (Fig. 1c). This was followed by AML, which grew by 108 percent from 9,400 cases in 1998 to 19,580 cases in 2018. Instances of CML grew by 96 percent from 4,300 in 1998 to 8430 in 2018, whereas ALL cases grew by 92 percent from 3100 in 1998 to 5,960 in 2018. (Fig. 1c). AML mortality was high at all times, rising from 6,600 cases in 1998 to 10,670 cases in 2018, a 62 percent increase (Fig. 1d). CLL and ALL mortality have been largely consistent over the last 20 years. Notably, CML mortality decreased from 2,400 cases in 1998 to 270 cases in 2011 (a 90 percent decrease), but CML fatalities began to rise again in 2018, reaching 1,090 cases (Fig. 1d).

In India, the number of cancer-related fatalities grew from 3,82,000 in 1990 (95 percent UI 351 000–412 000) to 813000 (767 000–850 000) in 2016. In 2016, India's crude cancer death rate was 61.8 (95 percent UI 58.3–646) per 100 000, up from 44.2 (40.6–477) in 1990. Throughout 31year, male cancer patients saw a 123 percent (95 percent UI 2.9–23.3) rise in age-standardised mortality rate, but female cancer patients had no significant changes. In 2016, there was no significant difference in the crude death rate across the ETL state groupings. Mizoram, Kerala, and Haryana had the highest crude death rates for both sexes in 2016, followed by Assam, Karnataka, Odisha, Uttarakhand, Meghalaya, and Himachal Pradesh. The northeastern states of Mizoram, Meghalaya, Arunachal Pradesh, and Assam had the highest age-standardised mortality rates.

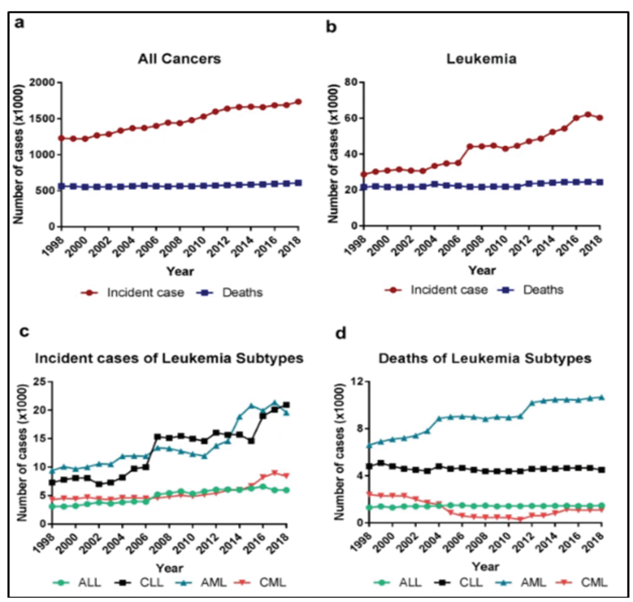

Figure 1. Shows the number of leukaemia diagnoses and fatalities in the United States from 1998 to 2018. (a, b) All cancers (a) and leukaemia (b) incident cases and fatalities (b). (c) Incidence instances of four main leukaemia subtypes. (d) Deaths from four leukaemia subtypes.

In 2016, leukaemia caused the most DALYs in boys and girls aged 0–14 in India, followed by brain and nervous system cancer. In 2016, female breast and cervical cancer DALY rates grew after 30 and declined after 60. In 2016, lung and stomach cancer DALY rates grew after 35 in men, while prostate cancer rose after 50. In 2016, GBD estimated that smoke, alcohol, and food caused the most cancer DALYs. They caused 109 %, 66 %, and 6 % of cancer DALYs.

In 2016, there were 34 000 incident leukaemia cancer cases in India (95 percent UI 30 000–38 000), with 105 000 prevalent cases (96 000–120 000). Between 1990 and 2020, the age-standardised incidence rate of leukaemia in India reduced by 161 % (95 percent UI 4.3–242). In India in 2016, leukaemia was responsible for the largest share of cancer DALYs (346 %) among children aged 0–14 years, which was comparable across boys and females. In 2020, the age-standardised incidence rate of leukaemia differed by 2.2 times among India's states. In 2020, the ETL state groups had comparable crude DALY rates for leukaemia. Delhi and Punjab had the highest incidence of leukaemia-related DALYs. The greatest and lowest state-specific DALY rates for leukaemia were separated by 2.5 times. In 2016, leukaemia was the third and fifth major cause of cancer mortality in men in Delhi and Punjab, respectively, while it was lower in other states.

3.2 Stomach Cancer

In India, the projected number of incident stomach cancer cases in 2016 was 75,000 (95 percent UI 73,000–78,000), with 1,12,000 prevalent cases (1,09,000–1,16,000). Between 1990 and 2020, India had a significant decrease in the age-standardised incidence rate of stomach cancer (397 %; 95 % UI 343–444). In 2016, stomach cancer was the fourth most common malignancy in both women and men in India. In 2020, the age-standardised incidence rate of stomach cancer differed by 12.5 times among India's states. Stomach cancer is the only cancer type for which declining rates were calculated in all states throughout the nation; females in Himachal Pradesh, Uttarakhand, Sikkim, and Delhi are the states that are included in this list had a fall of more than 50 %, while men in Maharashtra saw a decline of more than 50 %. The greatest and lowest state-specific DALY rates for stomach cancer were 13.1 times different. Mizoram, Arunachal Pradesh, and Jammu & Kashmir had the highest crude DALY rate. In 2016, stomach cancer was the leading or second leading cause of cancer mortality for females in 15 states and men in 18 states. Only a small percentage of the DALYs in India due to stomach cancer and leukaemia 2020 may be attributable to risk variables mentioned in GBD.

3.3 Breast Cancer

In India, the projected number of incident breast cancer cases in 2016 was 118 000 (95 % UI 107 000–130 000), with 98.1 % of cases being females and 526 000 (474 000–574 000) being prevalent. Breast cancer is the most common cancer among Indian women, with the highest overall incidence and prevalence of any cancer type. Between 1990 and 2020, the age-standardised incidence rate of breast cancer in females grew by 60 % (95 % UI 5.1–85.5), with increases reported in every state in the nation. In 2016, the age-standardised incidence rate of breast cancer in females differed by 3.2 times among Indian states. Breast cancer had the greatest crude incidence and DALY rates in the high ETL state group. The highest and lowest state-specific breast cancer DALY rates were 4.1 times different in 2016. Kerala, Punjab, and Tamil Nadu had the highest crude breast cancer DALY rates Delhi, Maharashtra, Karnataka, and Haryana are the states that come in second place in the higher-middle ETL group, after being in the high ETL group. Cancer deaths among women in 28 Indian states in 2016 were caused by breast cancer. High fasting plasma hyperglycaemia [49 %] and second-hand smoking [24 %] contributed to just a tiny percentage of breast cancer-related DALYs in India in 2016.

3.4 Lung Cancer

Lung cancer, tracheal cancer, and bronchus cancer can be referred to as "lung cancer" for simplicity's sake. Of the total number of lung cancer cases in India in 2016, there were 67,000 incident cases (95 % UI 63,000-72,000), with 72.2 % of those cases being men, and 74,000 prevalent cases (70,000-80,000). This condition ranked second among male cancers in 2020. In 2016, there was an 8-fold disparity between the sexes in the age-standardised incidence rate of lung cancer throughout the states of India. The male lung cancer incidence rates were highest in Kerala and Mizoram, whereas the female lung cancer incidence rates were highest in Mizoram and Manipur. The crude DALY rates for lung cancer in the highest and lowest states were 6.3 % and 6.2 %, respectively, in 2016. In 2016, the states of Mizoram, Kerala, Manipur, and Jammu & Kashmir had the highest crude DALY rates for lung cancer. For males, lung cancer ranked first or second in 2016 among cancer killers in 19 states, but for women, it was the case in just four states (Fig. 1). In 2016, 432 % of DALYs due to lung cancer were caused by tobacco use, whereas 43 % were caused by air pollution. Thus, tobacco use and leukaemia were the leading causes of cancer in GBD in India.

3.5 Lip and Oral Cavity Cancer

India has 113000 incident lip and oral cavity cancer cases in 2016 (95 % UI 1,06,000–1,18,000) and 3,97,000 prevalent cases. The age-standardised incidence rate of lip and oral cavity cancer in India dropped 64 % (95 % UI 0.4–18.6) between 1990 and 2020. Lip and oral cavity cancer was the most common malignancy among Indian men in 2016. Men had a considerably higher crude incidence rate. In 2016, there was a 5.1-fold difference between the sexes in the age-standardised lip and oral cavity cancer incidence rates throughout the states of India. Cancers of the mouth and lips showed the greatest DALY rates and crude incidences in the lower-middle ETL states. In 2020, there was a 5.5-fold difference between the greatest and lowest DALY rates for lip and oral cavity cancer among states. The greatest daily incidence rate of mouth and lip cancer is in Madhya Pradesh, followed by Kerala and Gujarat. In 2016, the leading cause of death for males in seven states in India was cancer of the mouth and lips. In 2016, smoking, drinking, and smokeless tobacco accounted for 332 %, 298 %, and 209 % of the DALYs in India related to lip and oral cavity cancer and leukaemia, respectively.

3.6 Pharynx Cancer other than Nasopharynx

In India, the number of incident pharyngeal cancer cases other than nasopharyngeal cancer cases was 65,000 (95 % UI 58,000–70,000) in 2016, with 702 % of the patients being males, and the prevalent cases being 1,52,000 (1,37,000–1,63,000). In 2016, the age-standardised incidence rate for other pharyngeal cancers differed 9.8 times across India's states for both sexes combined. The low ETL state group had a greater DALY rate for other pharyngeal cancer than the other ETL groups. In 2020, the greatest and lowest state-specific DALY rates for other pharyngeal cancers were 9.3 times different. Haryana has the highest DALY rate for other pharyngeal cancers, followed by Karnataka, Meghalaya, Assam, Rajasthan, and Himachal Pradesh. In 11 Indian states, other pharyngeal cancer was the primary or when it comes to men, cancer was the second largest cause of death in 2016.

In India, alcohol consumption was the top risk factor in GBD for other pharynx cancers in 2016, accounting for 30.1 % of all other pharyngeal cancer and leukaemia DALYs.

3.7 Colon and Rectum Cancer

In 2016, there were 63,000 incident colon and rectum cancer cases in India (95 % UI 58,000–66,000), with 1,85,000 prevalent cases (1,71,000–1,95,000). When compared to other ETL state groups, the high ETL had a greater incidence rate of colon and rectum cancer in both sexes. Over the course of the year 2020, the age-standardised incidence rate of colon and rectum cancer varied by 1.9 times between the states that make up India. It was 2.5 times greater than the difference between the highest and lowest state-specific DALY rates for colon and rectum cancer in the year 2016. Following Kerala, Mizoram, and Uttar Pradesh in terms of the number of DALYs that were caused by colon and rectum cancer, Odisha had the highest incidence of these cancers. From the third to the fifth largest cause of death from cancer, colon and rectum cancer was the leading cause of death in 24 states for females and 16 states for males. In India, dietary hazards were the greatest risk factor in GBD for colon and rectum cancer in 2016, accounting for 432 % of colon and rectum cancer and Leukaemia DALYs.

3.8 Cervical Cancer

In 2016, cervical cancer was the second most common malignancy in Indian women, with 77,000 incident cases and 2,88,000 frequent cases. India's age-standardised cervical cancer incidence rate dropped 397 % between 1990 and 2020. The 2020 age-standardised cervical cancer incidence rate in women differed 2.8 times between Indian states. States with the highest and lowest cervical cancer DALY rates differed by 3.4 times. In the year 2016, the state of Karnataka has the highest DALY rate for cervical cancer, followed by the states of Tamil Nadu, Chhattisgarh, Madhya Pradesh, and Maharashtra. Within the twelve states that make up India, cervical cancer was the second greatest cause of death for females.

India expects unsafe sex to cause all GBD cervical cancer DALYs by 2020. Since Population Attributable Fractions (PAF) of many risks may exceed 100 %, other undiscovered risk factors may also contribute to cervical cancer and leukaemia.

3.9 Esophageal Cancer

In 2016, there were 37 000 incident esophageal cancer cases in India (95 % UI 36,000–38,000), 60.8 % of which were men, and 41,000 prevalent cases (39,000–42,000). Between 1990 and 2020, the age-standardised incidence rate of esophageal cancer in India decreased significantly (312 %, 95 % UI 279–349). Over the course of the year 2020, the age-standardised incidence rate of esophageal cancer varied by a factor of 34 between the states of India. In terms of DALY rates for esophageal cancer, the highest and lowest state-specific rates were 33.8 times different from one another. The DALY rate for esophageal cancer was highest in the countries of Meghalaya, Assam, Mizoram, and Nagaland, which are located in the northeastern region. Esophageal cancer was either the major or second leading cause of death from cancer in two states for females and six states for males over the course of the study period. Smokeless tobacco, dietary risks, and smoking were the leading risk factors in GBD for oesophageal cancer and leukaemia in India in 2016. These three risk factors accounted for 22.6 %, 21.5 %, and 17.4 % of all DALYs associated with oesophageal cancer, respectively.

3.10 Brain and Nervous System Cancer

In 2016, India had 23,000 instances of cancer that occurred in the brain and nervous system (95 % UI 21,000–28,000), with 49,000 prevalent cases (44,000–57,000). In 2020, the age-standardised incidence rate of brain and nervous system cancer differed by 2.1 among India's states. Brain and nervous system cancer accounted for the second greatest percentage of cancer DALYs (16 %) among children aged 0–14 years in India in 2016, with comparable rates across males and girls. There was a difference of 2.6 times between the highest and lowest DALY rates for brain and nervous system cancer that were differed from state to state. Delhi has the highest DALY rate for brain and nervous system cancer or Leukaemia, followed by Sikkim. When compared to other high burden malignancies, mortality from brain and nervous system cancer and leukaemia were comparatively low in all states.

3.11 Prostate Cancer

With 33,000 (26,000–40,000) incident cases and 1,12,000 (87,000–1,37,000) prevalent cases, prostate cancer had the sixth highest incidence rate among men in India in 2016 (4.8 per 1,00,000, 95 percent UI 3.8–5.8). It is estimated that the age-standardised incidence rate of prostate cancer will increase by 298 percent between the years 1990 and 2020 (95 % UI 8.5–469). In 2020, this rate varied by 2.4 times throughout India's states. Kerala has the highest overall incidence rate of prostate cancer.

3.12 Larynx Cancer

In 2016, the incidence rate of laryngeal cancer among men in India was the sixth highest in the world (3.8 per 100,000, with a 95 % uncertain interval of 3.7–4.0).

In India, there were 31,000 (95 % UI 30,000–33,000) incident cases, with 83.5 % of them being males, and 96 000 (93 000–100 000) frequent cases. Between 1990 and 2020, the age-standardised incidence rate of laryngeal cancer in India reduced by 314 % (95 % UI 276–353). In 2016, this rate varied 3.3 times among India's states. Kerala had the highest crude incidence rate of laryngeal cancer among men in 2020, followed by Delhi, Haryana, and Assam. In India in 2020, smoking and alcohol use were the major risk factors for laryngeal cancer in GBD, accounting for 37.9 % and 172 % of laryngeal cancer and Leukaemia DALYs, respectively.

3.13 Liver Cancer

With a rate of 3.1 per 100,000 men with a 95 % confidence interval ranging from 2.9 to 3.2, India has the fifth highest incidence rate of liver cancer in this year (2016). In India, there were 30,000 incident instances, with 68.9 % of males, and 12,000 (11,000–14,000) common cases. The percentage of incident cases was 95 %, which is between 29,000 and 32,000. It is estimated that the age-standardised incidence rate of liver cancer increased by 322 % between the years 1990 and 2020 (95 % UI 11.4–413). During the year 2020, this rate differed 7.9 times between the states of India. As of 2016, the state of Arunachal Pradesh had the highest crude incidence rate of liver cancer among males, followed by the states of Kerala, Sikkim, and Mizoram following closely behind. It is possible that alcohol consumption in GBD will be responsible for 117 % of India's total DALYs in the year 2020 for liver cancer and leukaemia.

3.14 Ovarian Cancer

It was the sixth highest incidence rate among females in India in 2016, with 26,000 (95 % UI 24,000–27,000) incident cases and 76,000 (69,000–80,000) prevalent cases (40 per 1,000,000, 95 % UI 3.7–4.3). In 2016, the incidence rate of ovarian cancer was the sixth highest worldwide. The age-standardised incidence rate of ovarian cancer increased by 28.6 % during the years 1990 and 2020 (95 % UI 192–416). The rate was 3.7 times different in each of India's states in the year 2016. First place goes to Kerala, then Delhi, then Arunachal Pradesh, and finally Punjab. Kerala has the highest crude incidence. High fasting plasma glucose (GBD) risk factors may be responsible for a small percentage of the DALYs that are attributed to ovarian cancer in India in the year 2020.

3.15 Gallbladder and Biliary Tract Cancer

In India, gallbladder and biliary tract cancer had the tenth highest incidence rate among females in 2016 (26.6 per 1,00,000, 95 % UI 23.3–28.0). In India, there were 26,000 (95 % I 23,000–29,000) incident cases, 644 % of which were females, and 21,000 (18,000–23,000) prevalent cases. In the year 2020, this rate differed by a factor of 5.9 between the states of India. Assam and Delhi were the states that had the highest crude incidence of gallbladder and biliary tract cancer in females among the states that were included in the 2020 census. In 2020, high body mass index in GBD would be responsible for 91 % of gallbladder and biliary tract cancer and leukaemia DALYs in India.

3.16 Thyroid Cancer

Thyroid cancer was the tenth most common cancer in women in India in 2016 (25 per 1,00,000, 95 % UI 2.3–2.6). In India, there were 21,000 (95 % UI 20,000–23,000) incident cases, with 743 % of them being females, and 1,06,000 (1,01,000–1,15,000) frequent cases. Between 1990 and 2020, the age-standardised incidence rate of thyroid cancer rose by 25.6 % (95 % UI 126.6–523). In 2016, this rate varied 6.1 times among India's states. In 2016, In terms of the crude incidence rate of thyroid cancer in females, Kerala had the highest crude incidence rate, followed by Sikkim, Nagaland, and Goa. Only a modest percentage of thyroid cancer-related and Leukaemia -related DALYs in India in 2016 may be linked to GBD risk factors (high body-mass index).

4. DISCUSSION

From 1990 to 2020, there has been an upsurge in the number of new cancer cases and fatalities in India, as did cancer proportionate contribution to total DALYs and fatalities in the nation. Over a period of 26 year, the overall incidence, mortality, and DALYs from cancer grew significantly. However, there was no change in the age-standardised rates for both sexes combined, underscoring the role of population expansion and ageing in the country's rising cancer burden. During this time, the age-standardised cancer and leukaemia mortality rate rose for men, indicating gender inequalities. In every state of the nation, men had greater MI ratios than females.

Alterations in cancer literacy and the ageing of the population, diagnosis, healthcare access, and a number of risk variables are believed to be responsible for the patterns found the incidence rates of cancers that are particular to both genders and types over the course of time in India. We highlight some of the most important risk factors linked to India's highest cancer burden. Changes in lifestyle, such as a reduction in the consumption of salt-preserved foods, an improvement in the availability of refrigeration, and an increase in the intake of fruit, as well as a drop in the prevalence of smoking, could be ascribed to the considerable decrease in the age-standardised incidence rate of stomach cancer across the country[22-24]. Helicobacter pylori infection is still common among Indians; hence this is unlikely to be a cause in the decreased incidence of stomach cancer. A large increase in the age-standardised incidence rate of breast cancer in India is correlated with changes in particular risk factors throughout the course of time. These risk factors include being older at the time of the first birth, having fewer children, and having a higher prevalence of overweight and obesity[22,25,26].

The significant reduction in the age-standardised incidence rate of oesophageal cancer may be attributable in part to lower smoking prevalence during the previous 31 years and smokeless tobacco usage during the last 10 years[8,22,24]. The lack of change in the age-standardised incidence rate of lung cancer in India could be due to the mixed trends of the country's major risk factors, which include a decrease in smoking and household air pollution but an increase in ambient air pollution, as well as patterns of other unknown risk factors[22, 24]. The minor drop in the age-standardised incidence rate of lip and oral cavity cancer in India over the last decade might be attributed to a drop in the usage of smokeless tobacco in the country[22]. Cervical cancer declining age-standardised incidence rate might be negatively connected to the reproductive risk factors described above for breast cancer growth in 2018[25]. There is no evidence of increasing seroprevalence of HPV and its subtypes over time in India due to the lack of regular Human Papilloma Virus (HPV) testing. Although leukaemia has been linked to genetic, infectious, and environmental risks, the causes for the significant drop in India's age-standardised incidence rate from 1990 to 2020 remain unknown.

In respect to the patterns of some of the top malignancies, the interaction of the two risk factors that may be ascribed to the largest percentage of cancer DALYs in India, tobacco and alcohol, is fascinating. Both of these factors play a role, albeit to varied degrees, in the development of cancers that affect the palate and oral cavity, the oesophagus, the larynx, and the liver. Over the course of the period from 1990 to 2020, the age-standardised incidence rate of the first three types of cancer decreased in India, whereas the rate of liver cancer increased substantially. Alcohol consumption has increased in India throughout this time period, whereas the number of people smoking cigarettes has decreased[8, 22]. The decrease in the incidence rate of lip and oral cavity, esophageal, and laryngeal cancers could be partly attributed to a greater influence of tobacco than alcohol on these cancers, while the increase in the incidence rate of liver cancer could be attributed to a greater influence of alcohol than tobacco on this cancer, in addition to the trends of yet unknown other risk factors contributing to all of these can be attributed to a greater influence of tobacco than alcohol on this cancer. Collaborative multi-institutional cancer risk factor research may assist in closing knowledge gaps and lead to a better understanding of the causes of significant declines or increases in the incidence of various malignancies in different areas of India. To separate the contributions of population structure changes, risk factors, interventions, and other drivers to the patterns of India's main malignancies, detailed decomposition studies are required. The incidence rate of many forms of malignancies varies dramatically throughout India. Even within the same geographical area, such as between neighbouring northeastern states, major differences exist—for example, a 15-fold disparity in age-standardised nasopharyngeal cancer incidence rates between Nagaland and Tripura.

Since 2011, there has been no substantial change or association between the aging of the Indian population and all malignancies and occurrences, which is an unexpected conclusion. Breast and prostate cancer occurrences have been mostly stable or reduced since 2011, similar to other malignancies including ALL. In the aging population of India, we discovered an emerging pattern of fast increases in myeloid Leukaemia and CLL, but not other malignancies. Hao[38], *et al.* (2019) identified the significant aging-dependent Leukaemia trend alterations in this research published after 2011. As a result, the bulk of the effect of the WHO amendments has already been taken into account. Many intrinsic variables contribute to HSC aging, which pre-disposes HSC and committed myeloid progenitor cells to the accumulation of genetic and epigenetic changes, as well as the creation of pre-leukemic clones that eventually lead to malignant transformation. This might explain why CML and AML occurrences are more likely to be impacted by age. In contrast to myeloid leukaemia, Chronic Lymphocytic Leukaemia (CLL) is a disease that originates in mature B cells that have undergone differentiation. The accumulation of genetic and epigenetic changes that lead to clonal B cell proliferation is the basis for the molecular pathogenesis of Chronic Lymphocytic Leukaemia (CLL), which occurs in a manner that is age-dependent. Surprisingly, recent research found that in CLL patients, the ability to create clonal B cells had already been gained at the HSC stage. As a result, HSC aging may play a role in CLL start and progression. We believe that finding innovative ways to prevent or inhibit HSC aging will eventually aid in the prevention and treatment of myeloid leukaemia and CLL. In the future, more coordinated efforts will be required to better understand the processes of HSC aging and to discover innovative ways to avoid leukaemia.

5. FUTURE PERSPECTIVE PROGRAMS INITIATED BY INDIAN GOVERNMENT TO CONTROL CANCER AND ITS IMPACT

It was in 1975 when the government of India initiated the National Cancer Control Programme with the intention of providing tertiary care cancer hospitals and institutions with the resources necessary to implement evidence-based, systematic, and equitable strategies for the prevention of leukaemia, early detection, diagnosis, treatment, and palliation, despite the limited resources available[27]. Under this initiative, state cancer institutes and tertiary care cancer centres have been developed to increase cancer awareness and management at the state level[28]. Despite these efforts, the country's access to vital cancer therapy is limited. For example, there is a lack of radiation equipment, treatment delays, and regional disparities in the allocation of such resources[29]. During the year 2010, India initiated the National Programme for Control of Cancer, Diabetes, Cardiovascular Disease, and Stroke. Currently, cancer control initiatives are included in this overarching programme for the prevention and treatment of non-communicable illnesses[30]. In order to combat cancer, the national programme intends to target avoidable common risk factors through community-level screening that is both cost-effective and efficient for high-burden cancers. These screenings include clinical breast examinations, visual inspection with acetic acid for cervical cancer, and visual examinations for oral cancers[14]. These initiatives, however, face several obstacles, including a lack of skilled human resources, the follow-up of positive tests, prompt diagnosis, and well-tracked referral pathways[31]. Furthermore, several of the malignancies that cause the largest cancer burden in India, such as leukaemia, stomach, and lung cancers, have limited population-level screening options. The variability across the states in this research may thus be used to direct primary preventive efforts for these malignancies. Less invasive H pylori testing may be a cost-effective first-line test for referrals to more invasive endoscopic testing for early diagnosis of stomach cancer in secondary prevention. Colorectal cancer screening with fecal occult blood tests should also be investigated as a non-invasive, cost-effective option[32]. This systematic review and detailed analysis of the differences in the distribution and trends of cancer types throughout India might serve as a valuable reference for future cancer prevention and management planning. In addition, cancer registry coverage in rural regions and several big Indian states that do not presently have registries should improve. To understand the causes of the shifting patterns of various kinds of malignancies in India, further large-scale collaborative research is required.

Cancer patients in India face significant out-of-pocket costs[11, 33]. Some state's insurance programs, as well as a former national insurance plan, aimed to mitigate the effect on household [34-36]. The recently announced National Health Protection Mission (Ayushman Bharat) could lower the economic burden of cancer and other non-communicable illnesses in India by providing health insurance to 500 million low-income households[37]. It would be beneficial to guarantee that this health-protection program covers all key components of leukaemia and cancer treatment.

6. CONCLUSION

Finally, this article's detailed epidemiology of 28 types of cancer in every state of India over the last quarter-century shows significant differences between states for leukaemia and can be used as a reference for more targeted cancer control planning that matches state cancer patterns. The growing contribution of cancer to India's illness burden should encourage more systematic and large-scale methods to reduce cancer impact at the population level. Improved human resources and infrastructure for cancer and leukaemia prevention, screening, treatment, and palliative care, as well as proper financial protection for cancer care, should be part of these efforts. To reduce leukaemia cases, these new techniques should target the 10 cancers that cause the most DALYs in India: stomach, breast, lung, lip, and oral cavity, pharynx other than nasopharynx, colon, and rectum, leukaemia, cervical, esophageal, and brain and nervous system cancers. Myeloid leukaemia and Chronic Lymphocytic Leukaemia (CLL) cases grew quickly, with a clear association to population aging. Although the entire impact of the aging of the 'baby boomers' on cancer occurrences would not be known for another decade, the growth in myeloid leukaemia and CLL looked to outstrip that of other malignancies. As conditions and resources permit, other forms of cancer should be treated in India.

From 1990 to 2020, this research presents complete descriptive epidemiology of cancer and its heterogeneity across all Indian states. Over the last 31 years, India has led the way in leukaemia, establishing and expanding the National Cancer Registry Program (NCRP) under the Indian Council of Medical Research via a network of cancer registries that currently spans 23 states and union territories. The GBD approaches depend heavily on NCRP data from India, but they also employ data from all available data sources, including non-NCRP registries, SRS death cause data and other sources, and several variables to arrive at the best feasible estimates for states without registries. As a result, disparities between the GBD estimates and the NCRP numbers, which are based exclusively on population-based registries, are predicted. The GBD and NCRP methodologies have complementary goals and benefits. While the NCRP uses a standardised methodology developed by the WHO International Agency for Research on Cancer and Leukaemia, the GBD methodology uses a standardised approach that also incorporates other sources of data for estimations in all Indian states, including those without registries, such as Bihar, Chhattisgarh, Jharkhand, and Uttar Pradesh. The GBD approach is part of a wider total disease framework estimating procedure that permits comparisons of cancer burden to other illnesses, which has served to highlight cancer's growing contribution to India's disease burden over the last quarter-century. The conclusions in this study were made possible by the NCRP and GBD close partnership. It also emphasised the need to establish cancer in vast states in north India where none currently exists, as well as proper coverage of rural populations at the initial level. This is our brief overview of responsible factors for leukaemia cases in India and a major portion is waited for more research.

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