

Cancer at Ages 15–29 Years: The Contrasting Incidence in India and England

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Background. There has been a steady increase in published research from Europe and North America on the epidemiology of cancers in young people. There are limited data from the developing world. We contrast the incidence of cancer at ages 15–29 years in India and England. **Procedure.** Malignant neoplasms in those aged 15–29 years registered during 2001–2003 in five urban population-based cancer registries (PBCRs) of India and in eight PBCRs in England were included. Site-based classification was used. Age-standardized incidence rates were expressed per 100,000 person years. **Results.** In India, 4,864 (5.8%) of 84,450 cases and in England, 8,137 (1.2%) of 65,675 cancer cases occurred in those aged 15–29 years. For this age group, the incidence rate for males and females in India were 12.91 and 14.19, and in England were

27.75 and 28.88, respectively. In males aged 15–29 years, the three most common cancers in India were leukemia, lymphoma, and central nervous system tumors and in England were cancers of male genital organs, lymphoma, and leukemia. Cancers of female genital organs, breast, and leukemia were most common in females in India and cancers of female genital organs, lymphoma, and melanoma in England. For cancers of mouth, stomach, and gall bladder, the incidence was higher in India. **Conclusion.** Incidence of cancer at ages 15–29 years in England is higher at most sites than in India. Variation in environmental exposures between the two countries might be an explanation. Under-ascertainment of cases and gender bias in seeking healthcare may also influence reported incidence rates in India. Pediatr Blood Cancer 2012;58:55–60. © 2010 Wiley Periodicals, Inc.

Key words: adolescents; cancer incidence; developing world; England; young Adults; India

INTRODUCTION

In 2002, Birch et al. [1], defined the incidence of cancers in people 15–24 years of age in England using a morphology-based classification scheme. Subsequently, other countries in Europe have done similar analyses for their local populations using the same classification scheme [2,3]. Incidence data in this age group have also been published from USA although a site-based classification was used [4]. As a result of these studies from Europe and North America, our understanding of the cancers which occur in teenagers and young adults (TYA) has improved. However, there are little or no data on cancers in this age group from the developing world. Based on a single recent review with a more limited age range, the incidence of cancer in adolescents aged 15–19 years was reported to range from 9.5 to 25.5 per 100,000 person years across the world [5]. The highest incidence rates were reported from Australia and among Jews in Israel with the lowest in India and Japan.

We present here incidence rates of cancer among males and females aged 15–29 years (henceforth, referred as TYA) in India and contrast this with the rates for the same age range in England. Studying variations in cancer incidence in these age groups in different populations and geographical areas is likely to be informative as the relative exposures to potential environmental risk factors will be different.

METHODS

Data were obtained for the period 2001 to 2003 in the five urban population-based cancer registries (PBCR) of India (Bangalore, Bhopal, Chennai, Delhi, and Mumbai, shown in Figure 1, which cover 3.7% of the population of India and equate to 36 million person years) and eight regional registries in England (which cover the entire population and equate to 28 million person years) [6,7]. All primary neoplasms of malignant behavior, except non-melanoma skin cancer, registered for individuals 15–29 years of age were included. Cancer registration in India is active and data are collected from relevant hospital departments, pathology laboratories, and death certificates from the municipal corporation units.

Reliability of data and quality of registration are constantly monitored by re-abstraction and coding on a random sample of cases. Checks related to duplicate verification and matching with mortality records are also carried out by the individual registries. After this, data are sent to the Coordinating Unit at Bangalore where various range, consistency, and unlikely combination checks are carried out [6]. Completeness of population coverage by the registries does vary and has been estimated to be 72% in Bangalore, 100% in Chennai, and 78% in Mumbai [8].

Cancer registration in England is carried out by a network of eight population-based regional registries. Registration is coordinated by the Office for National Statistics in London, which maintains the national cancer registry covering all age groups. There is a high degree of case ascertainment and reviews have shown that registry records are largely complete, accurate, and reliable [9]. National population estimates by single year of age, gender, and calendar year are supplied by the Population Estimates Unit, Office for National Statistics. Annual mid-year estimates of population in England, based on census data together with information on births, deaths, and migration are very accurate on a national basis [9].

As available data in India were coded by site and not morphology, tumors in both countries were categorized based on International Classification of Diseases site codes [7]. Incidence rates were expressed per 100,000 person years and where appropriate, rates

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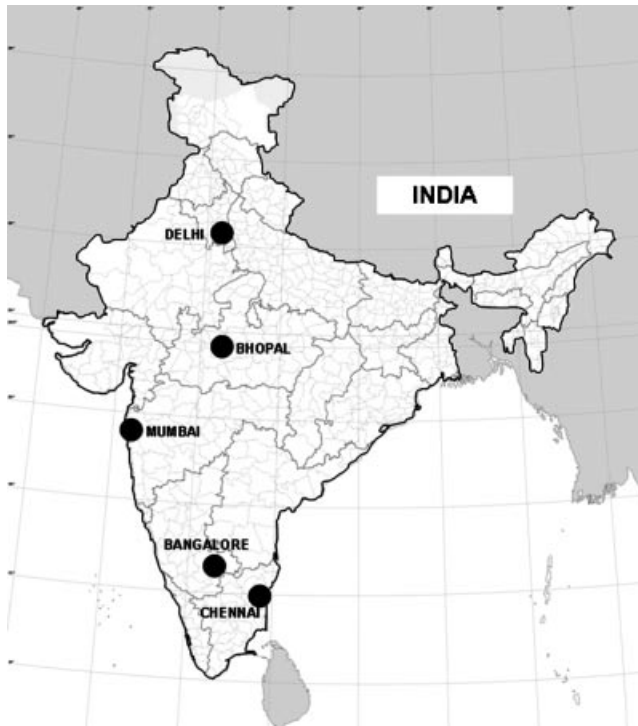


Fig. 1. Location of urban population-based cancer registries in India.

were adjusted to the world standard population using direct methods. *P*-values for variability in cancer-specific incidence rates by country for both males and females were calculated. R and Microsoft Excel were used for analyzing the data and producing tables and graphs.

RESULTS

During the period 2001–2003, 4,864 of the 84,450 overall cancer cases (5.8%) registered in the five urban cancer registries in India occurred in those aged 15–29 years (TYA). Two thousand five hundred fifty-nine were male (52.6%) and 2305 were female and the overall age-standardized incidence rates were 12.91 and 14.19 per 100,000 person years, respectively. Correspondingly, 8,137 of the 656,752 cases (1.2%) registered in England occurred in TYA. There were 3,992 males (49.1%) and 4,145 females and the overall age-standardized incidence rates were 27.75 and 28.88 per 100,000 person years, respectively. Further analysis by 5-year age groups showed that incidence rates in both sexes in both countries increased with age with the incline of slope steeper in females (Fig. 2). The result was that while for ages 15–19 years the incidence was higher in males, this pattern reversed and the incidence for those aged 25–29 years was higher in females.

Age-adjusted cancer incidence rates for all major sites and selected sub-sites are shown in Tables I and II. The three most common cancers in India in TYA males were leukemia, lymphoma, and central nervous system (CNS) tumors and in females cancers of the female genital organs, breast, and leukemia. In contrast, the three most common cancers in England in TYA males were those of the male genital organs, lymphoma, and leukemia and in females were cancers of the female genital organs, lymphoma, and melanoma. The incidence of melanoma in males in England was 61 times higher than the incidence in India and in females was 188 times higher. Sim-

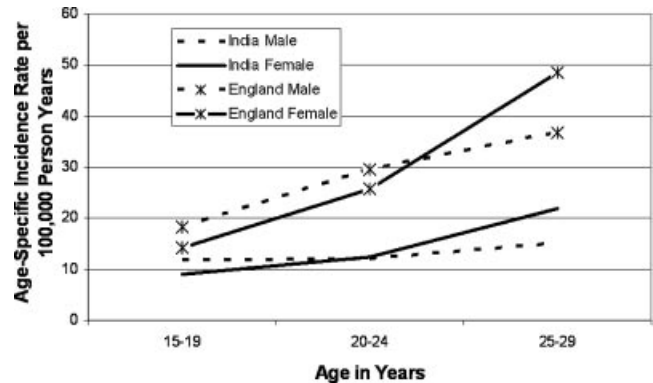


Fig. 2. Age- and sex-specific cancer incidence rates in those aged 15–29 years in England and India, 2001–2003.

ilarly, the incidence of testicular cancer was 14 times higher and of cancer of the cervix uteri 6 times higher in England. Cancer at all sites generally, had a significantly higher incidence in England. Notable exceptions to this pattern were cancer of the mouth (in males), stomach (in females), gall bladder (in males and females) and bone (in males) which had higher rates in India.

DISCUSSION

In this paper, we have contrasted the incidence of cancers in India and England in TYA. Our analysis shows that the incidence of cancer at these ages in England is around double that in India and the gap between the reported incidence rates in the two countries appears to increase with age. Similar patterns are observed when we contrast the incidence rates from India to published data from USA and other European countries [2–4]. The observed difference in incidence may be real but when interpreting these observations, one needs to consider a number of factors including under ascertainment of cases and gender bias in seeking health care which may influence reported incidence rates in India [8,10]. In addition, while data from England are national with high levels of ascertainment and completeness [9], the data from the Indian registries cover only 3.7% of the total Indian population. However, these registries are distributed across India and cover 42 million persons, 12.5% of the urban population. In this latter respect the population covered is more comparable to the English population since England is a densely populated industrialized nation. In terms of ethnic and religious sub-groups the populations covered can be considered as representative of India as a whole [6]. It is noteworthy that cancer in TYA as a proportion of cancer at all ages is five times higher in India than England despite the actual incidence being lower in India. This possibly reflects the higher percentage of young people in the population pyramid (31% of the population in India are TYA compared to only 19% in England).

Certain epithelial cancers which typically occur in older adults (lung, colorectal, breast, and ovarian cancer) have a higher incidence in the developed world which is well-recognized. This is explained by the prevalence of tobacco smoking and other western lifestyle-related exposures (high-caloric diet, low physical activity), together with differences in reproductive history (early menarche, late or no pregnancy) [11,12]. Our analysis shows that the incidence of lung, breast, colorectal, and ovarian cancer in TYA is higher in England than in India. TYA with these cancer will not have had the decades

TABLE I. Site-Specific Cancer Incidence Rates (Expressed Per 100,000 Person Years) and Male to Female Incidence Ratio in Those Aged 15–29 Years in England and India, 2001–2003

	India			England		
	Number	Incidence	Male:female	Number	Incidence	Male:female
All sites	4,864	13.51	0.9	8,137	28.33	1.0
Lip, oral cavity, pharynx	309	0.85	1.7	146	0.51	1.0
Tongue	51	0.14	2.0	37	0.13	1.1
Mouth	74	0.20	1.9	23	0.08	0.7
Salivary gland	71	0.20	1.1	41	0.14	0.8
Nasopharynx	58	0.17	2.6	38	0.14	1.7
Other	55	0.15	1.5	7	0.02	1.3
Digestive organs	490	1.33	1.0	352	1.22	1.0
Stomach	78	0.21	0.9	36	0.12	1.4
Colorectum	225	0.61	1.0	224	0.78	1.0
Liver	54	0.15	1.8	44	0.16	0.9
Gall bladder	44	0.12	0.7	6	0.02	3.0
Other	89	0.24	0.8	42	0.16	0.9
Respiratory and intrathoracic Organs	107	0.29	1.7	117	0.41	1.3
Lung	51	0.14	2.0	70	0.24	0.8
Other	56	0.15	1.5	47	0.16	2.3
Bone and articular cartilage	382	1.10	1.7	245	0.89	1.5
Melanoma	11	0.03	2.0	1003	3.44	0.5
Mesothelial and soft tissue	225	0.63	1.3	229	0.81	1.2
Mesothelioma	2	0.01		2	0.01	
Kaposi's sarcoma	0	0.00		21	0.07	1.3
Connective and soft tissue	223	0.62	1.3	206	0.73	1.1
Breast	347	0.02	0.0	398	1.34	0.0
Female genital organs	422	2.59		991	6.81	0.0
Cervix uteri	108	0.64	0.0	604	4.09	0.0
Ovary	257	1.60	0.0	328	2.32	0.0
Other	57	0.34	0.0	59	0.40	0.0
Male genital organs	142	0.70		1271	8.74	
Testis	126	0.63		1262	8.67	
Other	16	0.08		9	0.07	
Urinary tract	76	0.21	1.0	93	0.32	1.3
Eye	15	0.04	3.0	28	0.10	1.4
Central nervous system	491	1.53	1.3	562	1.98	1.3
Thyroid and other endocrine	292	0.80	0.2	403	1.39	0.3
Thyroid	279	0.76	0.2	391	1.35	0.3
Other	13	0.04	0.8	12	0.04	0.3
Lymphoma	633	1.77	1.8	1562	5.52	1.3
Hodgkin's lymphoma	255	0.72	1.7	982	3.48	1.2
Non-Hodgkin's Lymphoma	378	1.05	1.9	580	2.03	1.6
Leukemia	777	2.19	1.6	585	2.09	1.4
Lymphoid leukemia	250	0.72	1.7	232	0.85	1.7
Myeloid leukemia	421	1.18	1.3	338	1.19	1.2
Other	106	0.29	2.7	15	0.05	2.7
Other and unspecified	145	0.41	1.0	152	0.53	1.7

of tobacco, diet, reproductive, and other lifestyle exposures experienced by older adults. Genetic susceptibility may play a greater role in this age range [13]. In Britain, a relatively high proportion of predisposing mutations in BRCA1, BRCA2, and TP53 have been found in a series of breast cancer patients diagnosed at age 30 years or under [14], and of mismatch repair genes MSH2 and MLH1 in colorectal cancer patients aged less than 30 years [15]. The relative frequency of these high-penetrance mutations reported in Indian patients with these cancers is similar [16,17].

Although variation in low-penetrance cancer susceptibility genes could also play a role and needs to be explored in future studies, our observations imply that the differences seen in the incidence

of these cancers in TYA in India and England are more likely to be the result of differences in lifestyle-related factors. This is supported by studies of cancer incidence among populations of South Asian extract in England. Less than 4% of the UK population is of Asian extraction (1.8% Indian, 1.3% Pakistani, 0.5% Bangladeshi, and 0.4% other Asian). Analyses of cancer incidence among South Asians resident in England have shown that whereas overall rates for all cancers among all ages combined were lower in South Asians than non-South Asians these rates were higher than in the Indian sub-continent [18]. Furthermore, English South Asian rates for 0- to 29-year olds were similar or higher than non-South Asian rates [19]. A more recent study analyzed cancer incidence trends in the

TABLE II. Site- and Sex-Specific Cancer Incidence Rates (Expressed Per 100,000 Person Years) in Those Aged 15–29 Years in England and India, 2001–2003

	Male			Female		
	India	England	<i>P</i> -value	India	England	<i>P</i> -value
All sites	12.91	27.75	<0.0001	14.19	28.88	<0.0001
Lip, oral cavity, pharynx	1.04	0.52	<0.0001	0.62	0.50	0.15
Tongue	0.18	0.13	0.22	0.09	0.12	0.28
Mouth	0.26	0.06	<0.0001	0.14	0.09	0.27
Salivary gland	0.20	0.12	0.1	0.19	0.16	0.54
Nasopharynx	0.23	0.17	0.28	0.09	0.10	0.73
Other	0.18	0.03	<0.0001	0.12	0.02	0.0002
Digestive organs	1.31	1.22	0.45	1.34	1.22	0.25
Stomach	0.20	0.14	0.19	0.22	0.10	0.01
Colorectum	0.61	0.77	0.07	0.61	0.79	0.07
Liver	0.18	0.15	0.44	0.10	0.16	0.22
Gall bladder	0.10	0.03	0.005	0.14	0.01	<0.0001
Other	0.21	0.16	0.07	0.28	0.17	0.06
Respiratory and intrathoracic organs	0.36	0.46	0.25	0.21	0.36	0.02
Lung	0.18	0.21	0.45	0.09	0.27	0.0001
Other	0.18	0.25	0.21	0.12	0.11	0.31
Bone and articular cartilage	1.35	1.07	0.02	0.78	0.70	0.44
Melanoma	0.04	2.22	<0.0001	0.02	4.67	<0.0001
Mesothelial and soft tissue	0.71	0.87	0.09	0.53	0.75	0.02
Mesothelioma	0.01	0.01	0.75	0.00	0.00	—
Kaposi's sarcoma	0.00	0.08	<0.0001	0.00	0.06	0.0002
Connective and soft tissue	0.70	0.77	0.43	0.53	0.69	0.09
Breast	0.03	0.02	0.62	2.04	2.66	0.0003
Female genital organs				2.59	6.81	<0.0001
Cervix uteri				0.64	4.09	<0.0001
Ovary				1.60	2.32	<0.0001
Other				0.34	0.40	0.37
Male genital organs	0.70	8.74	<0.0001			
Testis	0.63	8.67	<0.0001			
Other	0.08	0.07	0.54			
Urinary tract	0.20	0.35	0.01	0.21	0.28	0.21
Eye	0.06	0.11	0.07	0.02	0.08	0.02
Central nervous system	1.53	2.25	<0.0001	1.17	1.71	<0.0001
Thyroid and other endocrine	0.33	0.63	<0.0001	1.38	2.17	<0.0001
Thyroid	0.29	0.61	<0.0001	1.34	2.11	<0.0001
Other	0.03	0.02	0.72	0.04	0.06	0.45
Lymphoma	2.22	6.21	<0.0001	1.21	4.81	<0.0001
Hodgkin's lymphoma	0.89	3.72	<0.0001	0.51	3.23	<0.0001
Non-Hodgkin's lymphoma	1.33	2.49	<0.0001	0.69	1.58	<0.0001
Leukemia	2.62	2.42	0.22	1.65	1.76	0.44
Lymphoid leukemia	0.88	1.06	0.12	0.52	0.62	0.19
Myeloid leukemia	1.33	1.28	0.72	0.99	1.11	0.29
Other	0.41	0.08	<0.0001	0.15	0.03	0.0002
Other and unspecified	0.40	0.66	0.001	0.41	0.40	0.93

city of Leicester, in the East Midlands region of England, where 22% of residents are of South Asian extract [20]. Overall cancer rates were lower in South Asians than in non-South Asians but younger South Asians were at somewhat increased risk compared with non-South Asians. Furthermore, across all ages incidence increased over time in South Asians but decreased in non-South Asians. This was accounted for by increases in lung and prostate cancer in men and colorectal and breast cancer in women. The pattern of cancers in South Asians was therefore becoming more like that in non-South Asians. These changes are consistent with the adoption of Western life-style among the South Asian community in England.

Differences in lifestyle can also explain the variation seen in the incidence of oral cancer in TYA in India and England. Chewing tobacco is a major causative factor responsible for Indians having among the highest rates of oral cancer in the world [11]. Tobacco consumption (predominantly in the oral form) begins in childhood in India and is more prevalent in males [21]. It is mistakenly believed to be good for the teeth and indeed to have medicinal properties [21]. Despite legislation prohibiting the use of tobacco as an ingredient in dental products, the practice continues [22].

In contrast to the above cancers, where the incidence is either higher in both younger and older adults in England (colorectal,

lung, breast, and ovarian cancer) or in younger and older adults in India (oral cancer), the incidence of cervical cancer is higher in TYA females in England (Table I), while it is much higher in older females in India [11]. This paradox probably reflects differences in sexual behavior and screening practices in the two countries. Since the introduction of national cervical screening programme in England the overall incidence of cervical cancer has halved [23]. The incidence is much higher in developing countries like India where no national screening programmes exist. As cervical screening in England starts at 25 years of age, there may be an artefactual higher incidence of cervical cancers in those aged 25–29 years of age compared with India, where cancers are only diagnosed when symptomatic. Although cervical cancer screening in India is not national policy and no organized screening programmes exist, trials of simple, and inexpensive screening methodologies have been conducted to assess their suitability and effectiveness in a low-resource setting. Two such trials were carried out in Kerala, in Southern India, and Osmanabad in Central India, respectively [24,25]. These trial areas do not overlap with those covered by the five urban cancer registries and will therefore have had no impact on cervical cancer incidence rates presented here. A third trial was conducted in Mumbai but included only women aged 35–64 years [26]. The interim results of these trials are promising and it is to be hoped that future introduction of more widespread screening programmes will have an impact on incidence and mortality.

The other cancers with significantly higher incidence in TYA in India are stomach cancer (females only) and gall bladder cancer. The higher incidence of stomach cancer in TYA females in India is unexpected. Despite a high prevalence of helicobacter pylori infection, reported stomach cancer rates in India are among the lowest in the world [27]. Within India, the overall incidence of gastric cancer is reported to be four times higher in Southern India compared with Northern India [28]. In our analysis, stomach cancer incidence in TYA in Bangalore (0.36 per 100,000 person years) and Chennai (0.32 per 100,000 person years) is twice that of other parts of India (Bhopal 0.15, Delhi 0.18, and Mumbai 0.13 per 100,000 person years). Higher intake of spicy food in Southern India is hypothesized to be associated [29,30], although there have been no epidemiological studies to verify this. Gall bladder cancer rates in North and Central India are among the highest in the world and long-standing cholelithiasis is a reported major risk factor [31]. Compared to England, gall stone disease in India starts at a younger age, has a higher prevalence and patients have a much longer median duration of symptoms at presentation [31].

Several non-epithelial cancers (melanoma, Hodgkin lymphoma, and CNS tumors) have higher incidence in England in TYA, and while in some cases a biological/behavioral explanation exists or is plausible, for others there is no clear explanation at present. The incidence of melanoma worldwide is related to sun exposure, although this association is complex. Chronic, continuous sun exposure seen in tropical countries like India is inversely associated with risk of melanoma [32] and increased melanin in dark-skinned individuals acts as a natural sun-protection factor [33]. On the other hand, intermittent sun exposure, which is seen at higher latitudes like England, and where frequency of fair-skinned people is greater, is positively associated with the risk of melanoma. In addition, sharp increases in the incidence of melanoma have been seen in TYA in England [34] which may be attributed to changing behaviors (increased travel and sunbathing, and use of sunbeds) which are more prevalent in young people [35–37].

Hodgkin lymphoma has a classical bimodal age distribution in developed countries [38]. The first incidence peak of Hodgkin lymphoma (mainly nodular sclerosis type) is seen in TYA and then again in the 8th decade of life. In contrast, in the developing world the first peak of Hodgkin lymphoma, mainly mixed cellularity type associated with Epstein–Barr virus, is more common in childhood. Delayed exposure to childhood infections and maturation of cell immunity as a result of less overcrowding in the developed world are the proposed explanations behind these observations [39].

An increase in the incidence of CNS tumors seen mainly in young people and the elderly has been observed all over the Western world in the 1970s–1990s. Much of the increase in incidence in the USA has been attributed to advances in neuroimaging, neurosurgery, and neuropathology, and to changes in registration practice [40–42]. Availability and use of similar resources are likely to be less widespread in India due to the cost and expertise needed and this may account for lower CNS cancer incidence rates. Additional evidence comes from the observation that the incidence of CNS tumors in England among children, TYA and older adults of South Asian and non-South Asian origin is not significantly different [18,19].

In conclusion, the incidence of cancer in TYA in England is generally higher at most sites compared with India. Notable exceptions to this pattern are cancer of the mouth, stomach, and gall bladder. Variation in environmental exposures between the two countries might explain the majority of the observations. Under ascertainment of cases and gender bias in seeking health care might also influence reported incidence rates in India. These patterns help us to identify cancers with a known etiology which are potentially avoidable. Societal initiatives including education and legislation leading to modification of behavior at the individual level should be able to help reduce the incidence of cancers of the oral cavity in India and cervical carcinoma and melanoma in England in TYA.

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