

## RESEARCH ARTICLE

# Cancers of the Young Population in Brunei Darussalam

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### Abstract

**Background:** Globally, the overall incidence of cancer is increasing as a result of ageing populations and changing lifestyles. Cancer is one of the leading causes of death, especially in the developed nations. Cancers affecting the young population are generally considered uncommon. This study assessed the demography and trends of cancers of the young in Brunei Darussalam, a small and developing Southeast Asia nation. **Materials and Methods:** All patients diagnosed with cancers between 2000 and 2012 were identified from the cancer registry maintained by the State Histopathology Laboratory. Cancers of the young was defined as any cancers diagnosed under the age of 40 years. Demographic data and the type of cancers were collected and analysed using SPSS Statistics 17.0. **Results:** Among the 6,460 patients diagnosed with cancer over the study period, 18.7% (n=1,205) were categorized as young with an overall decline in the proportion from 26.6% in 2000 to 18.8% in 2012 (p<0.001 for trend). Among all cancers of the young, the most common systems affected were gynecological (24.1%), hematological/lymphatic (15.8%), subcutaneous/dermatological/ musculoskeletal (10.5%), breast (10.5%) and gastrointestinal (9.9%). Overall, among the different systems, neurological (54.9%) had the highest proportion of cancers of the young followed by gynecological/reproductive (30.6%), hematological/lymphatic (39.9%), endocrine (38.7%), subcutaneous/dermatological/ musculoskeletal (22.3%) and the head and neck region (20.1%). There was a female predominance (66.9%) and the incidence was significantly higher among the Malays (20.1%) and expatriates (25.1%) groups compared to the Chinese (10.7%) and indigenous (16.8%) groups (p<0.001 for trend). **Conclusions:** Cancers of the young (<40 years) accounted for almost a fifth of all cancers in Brunei Darussalam with certain organ systems more strongly affected. There was a female preponderance in all racial groups. Over the years, there has been a decline in the overall proportion of cancers of the young. Selective screening programs should nevertheless be considered.

**Keywords:** Cancer - malignancy - young patient - trends - epidemiology - Brunei

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### Introduction

Cancer is reported to be the leading cause of disease and death worldwide, with approximately 14.1 million of new cancer cases and 8.2 million cancer deaths recorded in 2012 (IARC, 2012). In that year, an estimated 32.6 million were living with cancer (IARC, 2012). An estimated 57% of all new cancer cases and 65% cancer related deaths 2012 occurred in developing and underdeveloped nations (IARC, 2012). Generally, the incidence of cancers are still increasing especially in the less developed nation, like in South East Asia (Moore et al., 2010; Kimman et al., 2012) but for some cancers, the rates are actually declining due to improvement in standard of living and intervention such as screening programs.

Cancers are generally more common among the elderly populations and this is not unexpected given that age is one of the important risk factors for most cancers. However, cancers in the younger population are not

uncommon and are increasingly being reported. However, young cancers have been variably defined; some use age between 15 to 29, defined as adolescent or young adult cancers, other use age 39 or less, while studies looking at specific systems have use age 40 or below or 45 or below (Mitry et al., 2001; Pearce et al., 2005; Aben et al., 2012; Johnson, 2013; Hawk et al., 2014; Moon et al., 2014; Thangjam et al., 2014). Common cancers in both the adolescents and young adult population include tumors of the hematological or lymphatic system (lymphoma and leukemia), germ cell (including testicular cancer) and soft tissue or dermatological tumors (melanoma and sarcomas). However, other cancers such as breast, cervical, liver, thyroid and colorectal cancers have been reported in a proportion of the young population (National Cancer Institute, 2012), with some associated with poorer prognosis (Dozois et al., 2008; Thapa et al., 2013; Hajmanoochchri et al., 2014). This is a concern as this group of the population is one of the productive groups

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of the population.

Brunei Darussalam is a developing Southeast Asia nation with an estimated population of 415,717 (July 2012 estimate) with racial of Malays (66.3%), Chinese (11%), expatriate group (22%) and the smaller proportion of indigenous population. The 'Other' or 'Expatriate' group consisted mainly of working population in the age range of 18 to 45 years old. This group comprised of the foreign nationals: Southeast Asia, Indian subcontinents and small population of Caucasians. The population of Brunei Darussalam is still considered young with approximately 10% of the population older than 55 years old. It is important to be aware of the characteristic and epidemiology of any disease including cancers in order to allow planning of healthcare. To date, there is no published data looking at cancers of the young in Brunei Darussalam. The aims of this research were to study the incidence of various cancers of the young of the different organ systems and also the trend in Brunei Darussalam over a thirteen years period.

## Materials and Methods

**Study design:** This was a retrospective study looking at cancers of the young over a 13-year period from 2000-2012. Cancers of the young was defined as cancers diagnosed at age less than 40 years. We used this definition as we wanted to include in addition to the childhood and adolescent cancers, the group of population who are considered young for certain cancers (i.e. colorectal, stomach and breast cancers) and contribute economically to the country. Cases were identified from the Cancer Registry maintained by the Department of Pathology, RIPAS Hospital, located in the main tertiary government hospital. The Department of Pathology is the only state laboratory that handles all histology specimens for the whole country. The registry was reviewed and data on gender, age, race and the types of cancer were extracted. The study was approved by the Medical and Health Research and Ethics Committee (MHREC) of the institution.

**Categorization of cancers:** The cancers were categorized

into organ systems: neurological (central or peripheral), gastrointestinal (esophagus, stomach, small and large bowel, anal canal, pancreas, liver and biliary system), head and neck (eyes, ear, salivary glands, oropharynx or laryngeal structures), thorax (lung, pleura and mediastinal structures), male reproductive organs (prostate, testes and penis), gynecological or female reproductive organs (ovaries, fallopian tubes, uterus, cervix, vagina and vulva), urological (kidney, ureter, bladder and urethra), endocrine (thyroid, parathyroid, adrenal or extra-adrenal tumour), hematological/lymphatic, dermatological, subcutaneous and musculoskeletal system. Cancers of unknown primary was categorized as primary unknown or metastatic diseases.

**Data collection and analyses:** Data collected included patients' gender, age at diagnosis of cancer, racial groups and the types of cancer. The cancers were categorized into organ system as described. The data was entered into a data abstraction sheet and were then recorded into Microsoft Excel before importing them to Statistical Package for Social Sciences (SPSS) 17.0 statistical software to be analyzed. Distribution of young cancers was measured according to categorical variables such as age, gender, race and types of cancers. A p value of less than 0.05 was considered significant.

## Results

### *Demographic characteristics of all cancer patients*

A total of 6,460 patients were identified to have cancers between 2000 and 2012. Overall, the mean age of patients at diagnosis of cancer was 54.9±17.5 years with gender ratio of 55.1%; 44.9% (female: male). Male cancers patients were significantly older (mean age, 59.0±18.2) compared to female patients (51.7±16.2, p<0.001). The racial distribution was consistent with national breakdown, with a majority of Malays (74.1%), followed by the Chinese (17.4%). Females accounted for a higher proportion compared to males among the different racial groups except for the indigenous.

Among the systems, gastrointestinal or digestive cancers were the most common (20.7%), followed by

**Table 1. Demographic Characteristics of Overall Cancer Patients and Breakdown of Cancers of the Young**

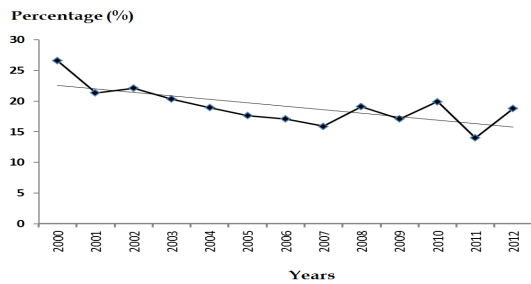
Variables	Overall Cancer Group n (%)			Cancer of the Young n (%)		
	Total	Male	Female	Total	Male	Female
Gender	5,252 (81.3)	2,859 (44.3)	3,599 (55.7)	1,205 (18.7)	399 (33.1)	806 (66.9)
Race						
Malay	4,772 (73.9)	2,059 (43.1)	2,713 (56.9)	961 (79.7)	317 (33.0)	644 (67.0)
Chinese	1,160 (18.0)	548 (47.2)	612 (52.8)	124 (10.3)	40 (32.3)	84 (67.7)
Indigenous	143 (2.2)	72 (50.3)	71 (49.7)	24 (2.0)	9 (37.5)	15 (62.5)
Others (foreign nationals)	383 (5.9)	180 (47.0)	203 (53.0)	96 (8.0)	33 (34.4)	63 (65.6)
Systems						
Gastrointestinal	1,337 (20.7)	803 (60.1)	534 (39.9)	119 (9.9)	60 (50.4)	59 (49.6)
Gynecologic/Female Reproductive	951 (14.7)	-	951 (100)	291 (24.1)	-	291 (100)
Breast	742 (11.5)	5 (0.7)	737 (99.3)	127 (10.5)	0 (0.0)	127 (100)
Thorax	586 (9.8)	256 (59.0)	240 (41.0)	25 (2.1)	11 (44.0)	14 (56.0)
Skin/soft tissue/ Musculoskeletal	565 (8.7)	343 (60.7)	222 (39.3)	126 (10.5)	62 (49.2)	64 (50.8)
Hematologic/Lymphatic	478 (7.4)	279 (58.4)	149 (41.6)	190 (15.8)	107 (56.3)	83 (43.7)
Head and Neck/Eyes/Ears	459 (7.1)	302 (65.8)	157 (34.2)	92 (7.6)	53 (57.6)	39 (42.4)
Male reproductive	302 (4.7)	302 (100)	-	27 (2.2)	27 (100)	-
Urological	238 (3.7)	154 (64.7)	84 (35.3)	17 (1.4)	344 (84.1)	65 (15.9)
Endocrine	194 (3.0)	45 (23.2)	149 (76.8)	75 (6.2)	14 (18.7)	61 (81.3)
Neurological	113 (1.7)	68 (60.2)	45 (39.8)	62 (5.1)	36 (58.1)	30 (41.9)
Primary unknown/metastatic disease	494 (7.6)	211 (42.7)	283 (57.3)	54 (4.5)	17 (31.5)	37 (68.5)

gynecologic cancers (14.7%) and breast cancers (11.5%). Apart from breast, reproductive and endocrine cancers, male had higher prevalence in the other systems cancer.

The demographic, gender, ethnic and system breakdown of the cancers diagnosed over the thirteen years study period are shown in Table 1.

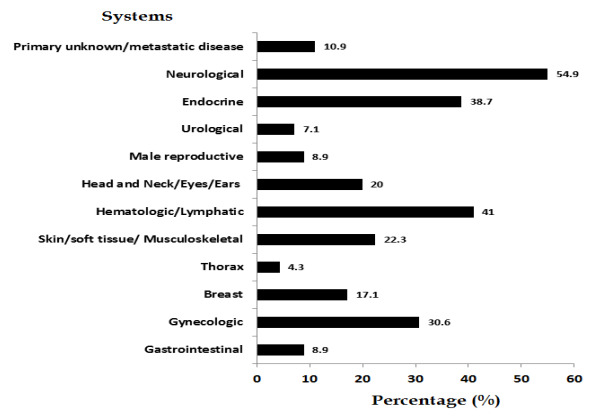
*Demographic characteristics of cancers of the young*

Overall, 1,205 patients (18.7%) were categorized as cancers of the young. Over the study period, the proportion of cancers of the young declined from 26.6% in 2000 to 14.0% in 2011 and 18.8% in 2012 (Figure 1).



**Figure 1. Annual Proportion of Cancers of the Young from 2000-2012 (n=1,205)**

Among all cancers of the young, the most common cancers were gynecologic cancer (24.1%), followed by hematologic/lymphatic (15.8%), skin/soft tissues/musculoskeletal (10.5%), breast (10.5%) and gastrointestinal cancers (Table 1). Excluding the gender specific systems, males predominate in most types of cancer with the exception of endocrine (81.3%), skin/soft tissues/musculoskeletal and thoracic cancers.



**Figure 2. Proportion in Percentages (%) of Cancers of the Young in the Various Systems**

**Table 2. Mean Age at Diagnosis of Cancers of the Various Systems among Young Patients**

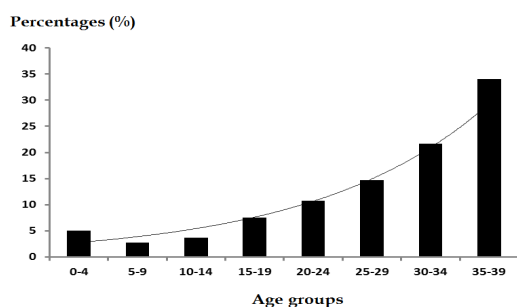
System	Overall	Mean Age Male	Female
Gastrointestinal	31.08 ± 7.30	31.65 ± 7.79	30.51 ± 6.79
Gynecological?Female Reproductive	32.37 ± 5.70	NA	32.37 ± 5.71
Breast	33.49 ± 5.34	NA	33.49 ± 5.34
Thorax	29.52 ± 6.63	27.09 ± 7.20	31.43 ± 5.68
Skin/Subcutaneous/Musculoskeletal	24.29 ± 10.42	23.97 ± 10.29	24.61 ± 10.61
Hematologic/Lymphatic	20.18 ± 11.79	19.35 ± 12.10	21.25 ± 11.37
Head And Neck/Eyes/Ears	29.98 ± 7.96	29.74 ± 9.04	30.31 ± 6.31
Male Reproductive	24.67 ± 11.03	24.67 ± 11.04	Na
Urological	25.59 ± 13.48	25.33 ± 13.83	26.20 ± 14.13
Endocrine	28.79 ± 6.77	25.64 ± 6.64	29.51 ± 6.65
Neurologic	17.45 ± 12.69	16.64 ± 12.02	18.58 ± 13.72
Primary Unknown/Metastatic Disease	30.61 ± 8.79	30.53 ± 8.06	30.65 ± 9.21
Overall	28.01 ± 10.04	24.50 ± 11.50	29.75 ± 8.74

\*Note: NA no cases diagnosed; Data presented as mean and standard deviation

**Table 3. Proportion of Cancers of the Young (Overall and between Genders) between Countries**

Country (Year)	Total cancers N	Total young cancers N (%)	Male n of young cancers/ Total cancers (%)	Female n of young cancers/ Total cancers (%)
United Kingdom (2011)	359,020	13,380 (3.73%)	5,520/186,810 (2.95%)	7,860/172,210 (4.56%)
United States (SEER data 2007-2011)		<20 year 1.0% 20-34 2.7% 35-44 5.2%		
Germany (2010)	477,303	16,903 (3.78%)	7,483 (2.96%)	9,420 (4.19%)
New Zealand (2010)	21,235	1,198 (5.64%)	526/11,068 (4.75%)	672/10,167 (6.61%)
South Australia (2009)	9,297	399 (4.29%)	182/5,349 (3.40%)	217/3,948 (5.49%)
Hong Kong (2010)	26,390	1,533 (5.80%)	527 (3.8%)	986 (7.59%)
South Korea (1999-2001)	310,715	33,433 (10.76%)	13,236 (7.48%)	20,197 (15.11)
South Korea (2011)	218,017	21,015 (9.63%)		
Japan (2008)	749,767	21,733 (2.89%)	7,653/437,787 (1.75%)	14,080/311,980 (4.51%)
Peninsular Malaysia (2003-2005)	67,783	12,088 (17.83%)	5,146 (17.38%)	6,942 (16.99%)
Thailand (2011)*	3,310	314 (9.49%)	111/1,317 (8.43)	203 (10.19%)
Brunei (2000-2012)	6,460	1,205 (18.7%)	399/1,993 (14.0%)	806 (22.4%)

\*Hospital based registry Only database or publication that provided age breakdown that provided data 39 years and below with the exception of the SEER data



**Figure 3. Proportion of Cancers of the Young by Age Group from 2000-2012 (n=1,205)**

The systems with the highest proportion of cancers of the young was neurological (54.9%), followed by hematologic/lymphatic, endocrine and gynecologic or female reproductive system. The proportion of cancers of the young in the various systems is shown in Figure 2.

Among the cancers of the young, there significantly more among female (22.4%, n=806) compared to male (14.0%, n=399) ( $p < 0.001$ ). The overall mean age of young cancer was  $28.01 \pm 10.46$  years, young among male patients ( $24.50 \pm 11.50$ ) compared to females ( $29.75 \pm 8.74$ ) ( $p < 0.001$ ). Among the age groups, the number of cancers increases exponentially with age (Figure 3). Neurologic and hematological/lymphatic had the lowest mean age (Table 2).

Apart from minor differences, the racial distribution was also found to be consistent with the national breakdown: Malays (77.5%), followed by Chinese (10.8%), others which consisted of foreign nationals (9.1%) and Indigenous (2.7%). Females appear to have the higher proportion than males among all the different racial groups.

## Discussion

Overall, cancers of the young accounted for 18.7% of all cancers diagnosed in Brunei Darussalam over the past 13 years. The reported rates of cancers of the young (<40 years) including childhood and adolescent/young adults cancers vary between countries (Table 3) (Cancer Incidence in Peninsular Malaysia, 2003-2005; Shin et al., 2005; Cancer in Germany 2007/2008; Cancer statistic in Japan, 2008; Government of South Australia, 2009; New registrations and deaths 2010; National Cancer Centre, 2011; Cancer Registration Statistics, 2011; Hospital Authority's Hong Kong Cancer Registry, 2014; Mehdi et al., 2014; National Cancer Institute, 2014; Parkin et al., 2014; SEERS, 2014; Wabinga et al., 2014). Generally, the proportions of cancers of the young correlate with the level of development of a country, with the lowest rates reported in the more developed nations and highest in the developing nation. In Southeast Asian developing nations, the rates ranged from 9.49% in Thailand (National Cancer Institute, 2014) based on a hospital based cancer registry, 17.83% in the Peninsular Malaysia (Cancer Incidence in Peninsular Malaysia, 2003-2005) to our high rates of 18.7%, the latter two based on National Registries. Even though the rates reported from developed nations are low (Shinet al., 2005; Cancer in Germany 2007/2008; Cancer

statistic in Japan, 2008; Government of South Australia, 2009; New registrations and deaths 2010; National Cancer Centre, 2011; Cancer Registration Statistics, 2011; Hospital Authority's Hong Kong Cancer Registry, 2014; Mehdi et al., 2014; Parkin et al., 2014; SEERS, 2014; Wabinga et al., 2014), the rates vary ranging from as low as 2.89% in Japan (Cancer statistic in Japan, 2008) to as high as 9.63% in South Korea (National Cancer Centre, 2011). However, the type of registries and the years studied likely influenced the rates. The higher rates reported from the SEER data was due to the inclusion of cancers in the 40-45 age groups (SEERS, 2014). Excluding this group would give a rate of less than 5%. Similarly the types of registry will also likely affect the results. The rate reported from the Thai study, a University Cancer Center based study will be influenced by referral and catchment biases (National Cancer Institute, 2014). It is unknown whether the rates will be higher in underdeveloped nations. However, it is likely to be lower than developing nations due to lower life expectancy and prevalent infectious diseases. Reported median age of diagnosis of breast cancers in the Middle East and some African Nation ranged from 43 to 52 years old (Mehdi et al., 2014), which are much younger than the rates reported by developed nations. The overall incidence of cancers will continue to increase as these nations develop and the proportions of cancers of the young will likely to increase before declining, following the patterns observed (IARC, 2012; Parkin et al., 2014; Wabinga et al., 2014).

The trend of the incidence of cancer of the young was found to be decreasing from 26.6% in 2000 to 18.8% in 2012 in our study. This is also seen in South Korea where the proportion had declined from 10.76% to 9.63% over ten years. (Cancer in Germany 2007/2008; Government of South Australia, 2009). The declining trends are likely the results of the ageing population, improvement in the standard of living, correlating with the level of development of the country. Changes in the population pyramid with larger older population reduce the proportion of cancers of the young even as the actual number of cases increases. Decline in rates of certain infectious diseases are likely to be important contributing factor in addition to life style changes and environmental exposures. Despite the decreasing trend we observed, it still represents a major concern given that a fifth to a quarter of all cancer cases occurred in an economically important group. Programs to increase healthcare providers' awareness are also important.

Among all systems, the most common cancers of the young were gynecologic or female reproductive cancers, followed by hematologic/lymphatic, breast, skin/soft tissue or musculoskeletal and gastrointestinal systems. Apart from the two cancers exclusive to female (breast and gynecologic) and exception of endocrine cancers, the other cancers of the young were more common among male. In the endocrine system, thyroid gland cancer, more common among women worldwide was the most common. For cancers of the hematologic/lymphatic and neurological systems, there was a U shaped distribution, common in childhood and older population (55 years above) whereas testicular cancer predominates in the

young population (20 to 40 years). Generally, our findings are similar to what have been reported in other countries with only difference in the absolute number of cases and proportions categorized as cancers of the young (Mitry et al., 2001; Shinet et al., 2005; Cancer in Germany 2007/2008; Government of South Australia, 2009; New registrations and deaths 2010; Cancer Registration Statistics, 2011; National Cancer Institute, 2012; Hawk et al., 2014; Hospital Authority's Hong Kong Cancer Registry, 2014; SEERS, 2014; Thangjam et al., 2014). As our nation develop, it is likely that the proportions will change and follow the patterns reported in some of the more developed Asian nations. However for some cancers such as cervical, breast and colorectal cancers, there incidence are increasing in our setting and the rates you cancers of the young in these system likely to decline at slower rates.

Gender distribution of cancers of the young is greatly dominated by female which accounted for two thirds (66.9%) of all the young cancers. This is in contrast to the gender distribution for overall cancers where female accounted for 55.7%. The main reason for this is that certain cancers exclusive to women such as breast and gynecological cancers were common. Our finding of female predominance in cancers of the young is similar to what have been reported from other countries both developed and developing nations (Mitry et al., 2001; Shinet et al., 2005; Cancer in Germany 2007/2008; Government of South Australia, 2009; New registrations and deaths 2010; Cancer Registration Statistics, 2011; National Cancer Institute, 2012; Hawk et al., 2014; Hospital Authority's Hong Kong Cancer Registry, 2014; SEERS, 2014; Thangjam et al., 2014). Interestingly, the rate was slightly among men in peninsular Malaysia (Hospital Authority's Hong Kong Cancer Registry, 2014). However, there were far more cancers diagnosed in women reported in this registry.

The mean age of diagnosis of cancers of the young was  $28.01 \pm 10.46$  years, ranging from  $17.45 \pm 12.69$  in the neurological system to  $33.49 \pm 5.34$  for breast cancers. Overall, cancers of the young among male were younger compared to their females counterpart. This was true for nearly all the systems with the exception of the gastrointestinal tract. In cancers of the gastrointestinal system, males were slightly older. Despite this, the overall differences between the genders and systems were minor. The most obvious difference was in the reproductive and the endocrine systems. Male young reproductive cancers were diagnosed much younger ( $24.67 \pm 11.04$  years) compared to female reproductive (gynecological) system, ( $32.37 \pm 5.71$  years). In our population, the overall mean age of diagnosis for all cancers and the various systems were generally younger compare to the Western or more developed Asian populations. This is also true for other less developed nations.

With the exception of cancers common to childhood, the mean ages of diagnosis for most cancers were over twenties, which make certain interventions such as educational awareness and even selective screening programs easier to implement and to be understood by the general public. Inclusion of awareness education targeting the tertiary education levels, the work force

(private or government employees) through inclusion into education syllabi or frequent public educations through frequent health promotions lectures, health awareness of these common cancers including cancers of the young and the various methods of detections including self-examinations (i.e. self-breast examination) and available screening programs. However, the levels of uptake for existing programs remain poor. A survey done in our local setting in 2008 showed that the rate of women getting screened for cervical cancers was less than 30%. Uptake for mammography screening also remains poor. Therefore, more needs to be done to increase public awareness and uptake in screening programs.

In conclusion, this is the first study to look at cancers of the young in Brunei Darussalam which showed that female predominate, mainly due to the large number of cancers exclusive to female; breast and gynecologic reproductive system. Generally, for most system, male predominated. Cancers of the young are common in developing nations and in Brunei Darussalam, the proportion of cancers of the young is declining. Despite it is still a major concern, as approximately a fifth of our cancers are diagnosed in the group of patient who are young and economically important to the country.

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