RESEARCH ARTICLE

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Epidemiology of Nasopharyngeal Carcinoma in Sarawak, East Malaysia

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Abstract

Objectives: This analysis provides an epidemiological update for nasopharyngeal carcinomas the state of Sarawak and an analysis of the trend over a 20 years period. **Method:** Data between 1996 to 2015 from a population-based cancer registry in Sarawak Malaysia was analyzed. Crude incidence rates and age-standardized rates (ASR) were calculated and compared between ethnic groups and locations (administrative division) and Joinpoint regression analysis was done to analyze trends. **Results:** A total of 3643 cases of NPC were recorded with male to female ratio of 2.5:1. Annualised age-standardized incidence rates able 2) for men is 13.2 cases per 100,000 population (95% CI: 12.6, 13.7) and for women is 5.3 cases per 100,000 population (95% CI: 5.0, 5.6). The highest incidence rates were reported among the Bidayuh population and it ranks among the highest in the world. Trend analysis noted an overall reduction of cases, with a significant decrease between 1996 and 2003 (annual percentage reduction of incidence by 3.9%). Analysis of individual ethnic groups also shows a general reduction with exception of Iban males showing an average 5.48 per cent case increase between 2009 to 2015, though not statistically significant. **Conclusion:** Comparing the incidences with other registries, the Bidayuh population in Sarawak remained among the highest in the world and warrants close attention for early screening and prevention strategies.

Keywords: nasopharyngeal- npc- epidemiology

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Introduction

Nasopharyngeal carcinoma (NPC) is a tumour that involves epithelial cells in the nasopharynx. It is usually asymptomatic until spread to regional lymph nodes, with common presentations such as nasal obstruction or bleeding, changes in hearing, headaches or neck swellings (Eu and Loh, 2021). Radiotherapy is the main treatment for cases without metastases.(Malaysia Health Technology Assessment Section, 2016). Studies have suggested strong links to heredity factors, smoking, as well as cultural practices such as the consumption of salted preserved foods (Yong et al., 2017).

Worldwide cases of NPC increased from 86,500 in 2012 (0.6% of all cancers) to 129,000 in 2018 (0.7% of all cancers) to more than 133,000 cases 2020. However, more than two-thirds of these cases were reported in east and southeast Asia. The World Cancer Research Fund International reported in 2020, 8 countries from Southeast Asia were in the top 10 nations in terms of age-standardised rates (Chen et al., 2019; Chua et al., 2016; Parkin et al., 2005).

In Asia, a few regions had reported particularly high incidences of NPC. Southern China noted a high incidence of NPC in a cohort study in Guandong province, where the age-standardized rates (ASR) were 30.3 cases per 100,000 population for men and 13.1 cases per 100,000 population for women (Zhang et al., 2015). In Hong Kong, the ASR in 2019 were 10.9 cases per 100,000 population for men and 3.0 cases per 100,000 population for women (Hong Kong Cancer Registry, 2021). Singapore reported ASR (2006-2010) of 9.5 cases per 100,000 population for men while the rates for women were not reported as being within the top 10 cancers (Teo and Soo, 2013).

The Malaysia National Cancer Registry Reports for 2007-2011 and 2012-2016 had NPC ranked as the fifth most common cancer among Malaysians, with ASR (2012-2016) of 5.2 cases per 100,000 population for men and 1.9 cases per 100,000 population for women. The state of Pahang reported lower ASR (2012-2017) of 2.4 cases per 100,000 population for men and 0.9 cases per 100,000 population for women, with patients of Chinese ethnicity showing higher rates compared to local natives (Bumiputeras) (Ahmad et al., 2021). Meanwhile, the state of Sabah reported higher than national figures with ASR (2015-2019) of 5.6 cases per 100,000 population for men and 2.3 cases per 100,000 population for women, with the highest incidences among patients of Dusun ethnicity,

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followed by those of Chinese and Kadazan ethnicities (Wong et al., 2021). A previous study in Sarawak has noted an ASR (2004) of 13.5 cases per 100,000 population for men and 6.2 cases per 100,000 population for women, with the Bidayuh ethnicity recording an ASR of 31.5 cases per 100,000 population for men and 11.8 cases per 100,000 population for women (Devi et al., 2004).

This study provides an updated ASR of NPC in Sarawak and compares ethnic groups and divisions, and also looks at the trend of cases over the period.

Materials and Methods

Setting and Data Collection

Sarawak is a state in East Malaysia located on the island of Borneo with a land area of 124,450 square kilometres and had a population of 1.64 million in 1990 which grew to 2.45 million in the 2020 census (Department of Statistics Malaysia, 2022). Administratively, the state is divided into eleven divisions which in turn consist of 41 administrative districts. Sarawak's Gross Domestic Product was reported to be RM 121,414 million in 2016 with a growth rate of 1.9%. The largest share comes from Services (34.4%), followed by Manufacturing (27.7%), Mining and Quarrying (21.2%), Agriculture (13.5%) and Construction (2.7%) (Department of Statistics Sarawak, 2015).

The population in Sarawak consists of over 27 different ethnic and sub-ethnic groups, each with its unique language, food and lifestyle(Sarawak Government, 2010). As of 2017, the largest ethnic groups are the Iban (28.6%), Malay (22.9%), Chinese (22.4%), Bidayuh (5.1%) and Melanau (5.1%) (Department of Statistics Malaysia, 2022). The ethnic composition may differ greatly between districts and thus it is expected that the reported rates of NPCs would vary. Sarawak has previously reported the highest incidence rates of NPC, particularly among the Bidayuh ethnic population (Chang and Adami, 2006; Linton et al., 2021). Therefore, it is of great interest to identify areas with higher risks to focus prevention and screening efforts among the population.

Data collection was based on the Sarawak Cancer Registry which was set up in 1996 as the regional population-based registry for patients with cancer. Passive data was collected from notification of cases from government and private healthcare centres upon diagnosis, as well as causes of death extracted from the National Registration Department. Active data collection was also done with tracing case notes from reporting centres and checking against existing cases in the registry to avoid duplication. The registry also captures data from death reports that report cancer as a contributing factor.

The diagnosis of nasopharyngeal carcinoma was classified according to the 10th revision of the International Classification of Diseases (ICD-10) according to the location of the tumour, from C11.0 (superior wall) to C11.8 (overlapping lesions) and C11.9 (unspecified). Data were entered and managed with the CanReg software, which is an open-source tool from the International Association of Cancer Registries, with the latest version being CanReg5.

For this study, data for notified new cases of NPC diagnosed between 1996 and 2015 was extracted from the Sarawak Cancer Registry for analysis. Patients were identified based on registry registration numbers so as not to compromise their confidentiality. Case location is based on the eleven administrative divisions in the state of Sarawak to enable comparison over time. The population census data were obtained from the Department of Statistics Malaysia.

Statistical methods

The age-standardized rates (ASR) were calculated using the world standard population provided by the World Health Organization (Ahmad and Pinto, 2001) expressed per 100,000 population. Differences between groups were analyzed with negative binomial regression against reference groups, using STATA software. Trend analysis was conducted using the Jointpoint Regression Program version 4.9.10 from National Cancer Institute to analyze the changes in trends according to ethnic group and gender.

Results

Between 1996 to 2015, a total of 3,643 cases of NPC were recorded. Table 1 shows the distribution of cases by

Table 1. Demographic Data of NPC Patients in Sarawak (1996-2015) which were Included in the Analysis (n=3,643)

Demographic Data	Number	%
Sex		
Men	2,604	71.5
Women	1,039	28.5
Age group		
0 to 19 years	115	3.2
20 to 39 years	790	21.7
40 to 59 years	1,908	52.4
60 years and above	830	22.8
Ethnicity		
Iban	1,169	32.1
Chinese	1,022	28.1
Bidayuh	629	17.3
Malay	477	13.1
Others	346	9.5
Division		
Kuching	877	24.1
Miri	526	14.4
Samarahan	515	14.1
Sibu	427	11.7
Sarikei	191	5.2
Bintulu	179	4.9
Sri Aman	174	4.8
Kapit	137	3.8
Betong	109	3
Limbang	70	1.9
Mukah	68	1.9
Undetermined	370	10.2

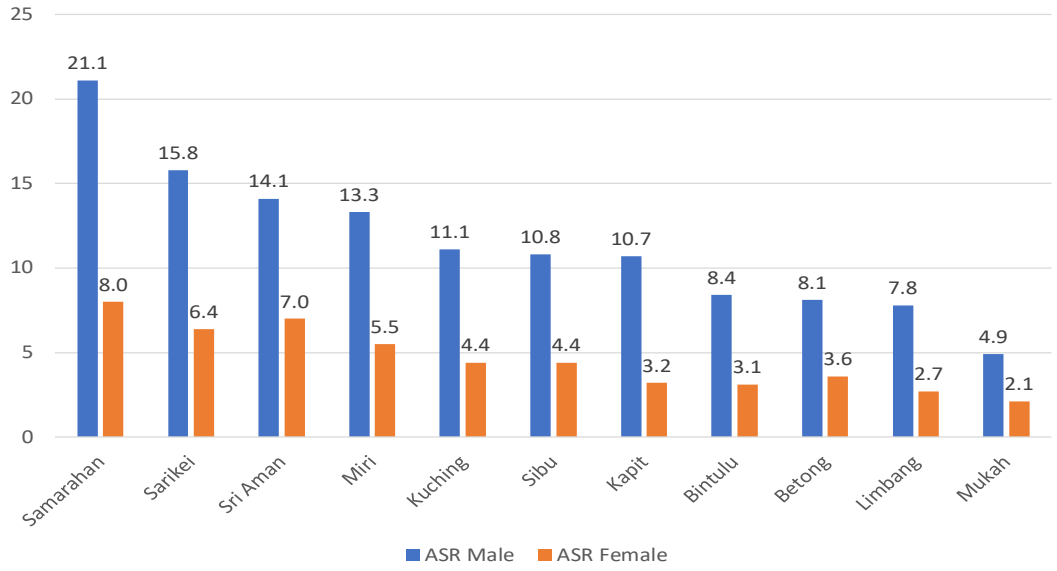

Figure 1. Annualised ASR for NPC (Per 100,000 Population) by Gender for Each Division in Sarawak, 1996-2015

gender, age group, ethnicity and division. There were 2.5 male cases for every female case, most of the patients were in the age group of 40 to 59 years old, and a majority of the cases were of the Iban ethnicity (32.1%) and Chinese ethnicity (28.1%), followed by Bidayuh ethnicity (17.3%) and Malay ethnicity at (13.1%).

The annualised ASR for men was 13.2 cases per 100,000 population (95% CI: 12.6, 13.7) and for women was 5.3 cases per 100,000 population (95% CI: 5.0, 5.6). The highest incidence rates were noted among Bidayuh ethnicity where men had an ASR of 27.8 cases per 100,000 population (95% CI: 25.1, 30.4) while the ASR among women was 11.6 cases per 100,000 population (95% CI: 9.8,13.2). The annualised ASR by division and gender is shown in Figure 1, where the division of Samarahan had more cases compared to the other divisions (ASR of 21.1 cases per 100,000 population for men and 8.0 cases per 100,000 population for women).

Comparing the group's annualised incidence rates, negative binomial regression values are in Table 2, with males with 2.528 times the IRR (95% CI: 2.133 to 2.997), higher ages showing a significant increase in Incidence Risk Ratio (IRR) and Bidayuh with the highest IRR among the ethnic groups as well as Samarahan showing significantly higher IRR compared to Kuching. All variables were also included in the multivariable analysis, with the same factors remain statistically significant.

Jointpoint regression analyses for ethnicity and gender are shown in Table 3 and Figure 2. Overall, there was a sharp decrease in cases from 1996 to 2003 with an annual reduction of 3.9 per cent, while there were no significant changes between 2003 to 2015 (APC -0.17). Analysis of individual ethnic groups also shows a general reduction, with exception of Iban males showing an average 5.48 per cent case increase between 2009 to 2015, though not statistically significant. The age groups of 40 to 59

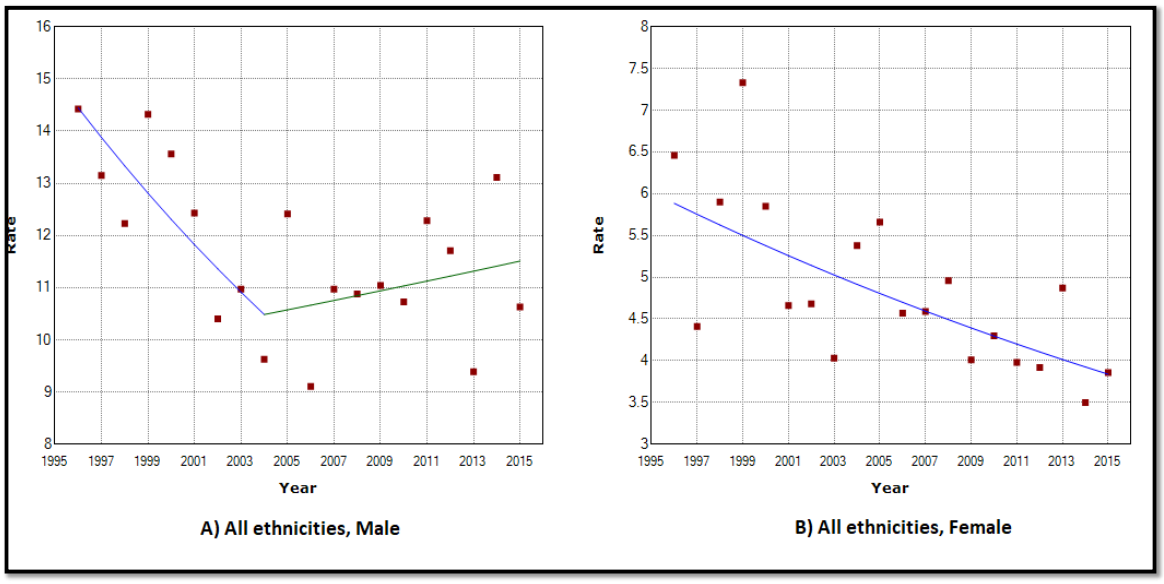

Figure 2. Joinpoint Regression Chart for All Ethnicities, by Gender

Table 2. Negative Binomial Regression to Compare Crude Incidence Rates between Demographic Groups (Multivariable) for NPC in Sarawak (1996-2015)

Demographic groups	Crude Incidence Rate	Univariate				Multivariate			
		Incidence Rate Ratio	95% CI for IRR	Std Err	p value	Incidence Rate Ratio	95% CI for IRR	Std Err	p value
Years									
1996-2000	1.97	1.58	1.239, 2.010	0.195	<0.001	1.689	0.000,1.489	0.109	<0.001
2001-2005	1.62	1.293	10.14, 1.650	0.161	0.038	1.357	0.000, 1.542	0.089	<0.001
2006-2010	1.51	1.068	0.837, 1.363	0.133	0.597	1.098	0.965, 1.250	0.073	0.157
2011-2015	1.56		(base group)				(base) group)		
Sex									
Men	2.32	2.528	2.133, 2.997	0.219	<0.001*	2.334	2.133, 2.997	0.219	<0.001*
Women	0.96		(base group)				(base group)		
Age group									
0 to 19 years	0.06		(base group)				(base group)		
20 to 39 years	0.59	9.748	7.617, 12.476	1.227	<0.001*	9.936	7.978, 12.376	1.113	<0.001*
40 to 59 years	2.17	33.596	26.465, 42.648	4.09	<0.001*	33.701	27.260, 41.665	3.647	<0.001*
60 years and above	2.37	38.685	30.218, 49.526	4.876	<0.001*	38.199	30.661, 47.591	4.284	<0.001*
Ethnicity									
Iban	1.76	1.564	1.208, 2.024	0.206	0.001*	1.689	1.462, 1.952	0.125	<0.001*
Chinese	1.8	1.329	1.014, 1.742	0.183	0.04*	1.341	1.152, 1.560	0.108	<0.001*
Bidayuh	3.42	2.696	1.989, 3.652	0.418	<0.001*	2.845	2.390, 3.387	0.253	<0.001*
Malay	0.92		(base group)				(base group)		
Melanau	0.61	0.466	0.315, 0.688	0.093	<0.001*	0.621	0.459, 0.839	0.096	0.002
Others	1.81	1.337	0.972, 1.837	0.217	0.074	1.781	1.448, 2.192	0.188	<0.001*
Division									
Kuching	1.41		(base group)				(base group)		
Miri	1.68	1.164	0.833, 1.624	0.198	0.373	1.318	1.124, 1.546	0.107	0.001*
Samarahan	2.44	1.685	1.202, 2.361	0.29	0.002*	1.443	1.233, 1.689	0.116	<0.001*
Sibu	1.44	0.857	0.603, 1.217	0.153	0.389	1.222	1.031, 1.448	0.106	0.021
Sarikei	2.06	0.892	0.612, 1.299	0.171	0.55	1.192	0.974, 1.460	0.123	0.089
Bintulu	1.07	0.637	0.440, 0.920	1.12	0.016*	0.901	0.735, 1.106	0.094	0.32
Sri Aman	1.84	0.986	0.666, 1.460	0.197	0.944	1.259	1.016, 1.560	0.138	0.035
Kapit	1.22	0.91	0.607, 1.364	0.187	0.649	0.911	0.721, 1.151	0.109	0.434
Betong	1.01	0.667	0.439, 1.014	0.142	0.058	0.906	0.715, 1.150	0.11	0.417
Limbang	0.88	0.513	0.334, 0.790	0.113	0.002*	0.64	0.473, 0.849	0.095	0.002*
Mukah	0.64	0.612	0.399, 0.938	0.133	0.024*	0.942	0.718, 1.238	0.131	0.671

*Statistically significant difference when compared to base group

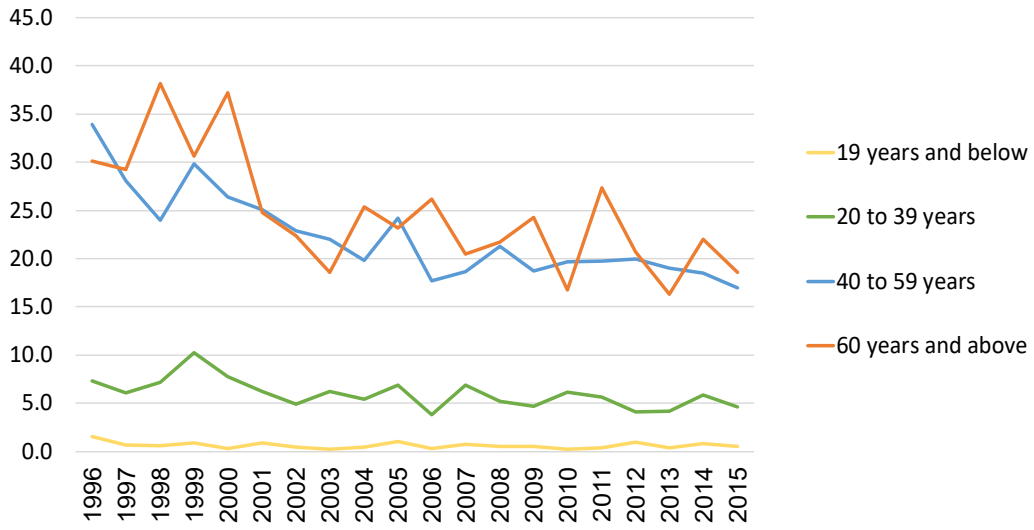

Figure 3. Trends of Crude Incidence Rates for NPC According to Age Groups

Table 3. Trends of Crude Incidence Rate of NPC by Ethnic Group, 1996-2015

Ethnic	Gender	Trend 1 years	APC	Trend 2 years	APC	AAPC**
All	Both	1996-2003	-3.90*	2003-2015	-0.17	-1.6*
	Male	1996-2004	-3.92*	2004-2015	0.85	-1.2*
	Female	1996-2015	-2.22*			
Iban	Both	1996-2015	-1.1*			
	Male	1996-2009	-2.35*	2009-2015	5.48	0.1
	Female	1996-2015	-2.6*			
Chinese	Both	1996-2015	-2.1*			
	Male	1996-2015	-1.7*			
	Female	1996-2015	-2.7*			
Bidayuh	Both	1996-2015	-1.0*			
	Male	1996-2015	-2			
	Female	1996-2015	-1.3*			
Malay	Both	1996-2015	-0.7			
	Male	1996-2015	-1.2			
	Female	1996-2015	0.4			
Others	Both	1996-2015	-0.8			
	Male	1996-2015	-0.7			
	Female	1996-2015	-4.2			

*Indicates Annual Percent Change (APC) is significantly different from zero at the alpha= 0.05 level; **AAPC, Average Annual Percent Change, when 1 or more joints in trend line

year olds and those 60 years and above had also shown a reducing trend for incidence rates (Figure 3).

Discussion

High rates among Bidayuh population

The Bidayuh has a higher incidence of NPC and there had been hypothesized links to risk factors such as genetics, diet, smoking practice and environmental exposures (Linton et al., 2021). Future cohort studies can be planned to look more closely into the factors and ways to promote early screening among this group.

Comparing with data from Cancer Incidence in Five Continents

To compare with other states and nations using the data from Cancer Incidence in Five Continents listings, the ASR was recalculated for the period 2008-2012. The general population in Sarawak showed an ASR of 11.8 cases per 100,000 population among men and 4.5 cases per 100,000 population among women. Meanwhile, the ASR among Bidayuh males and females for the same period were 23.8 cases and 9.0 cases per 100,000 population respectively, which is slightly more than double the rates for the general population. Comparing with available data from the state of Penang, both states had similar general population ASR with Penang recording a slight lower ASR of 10.6 cases per 100,000 male population and 3.3 cases per 100,000 female population. However Chinese in Penang recorded a higher ASR of 16.1 (compared to 11.9 in Sarawak) cases per 100,000 male population and ASR of 4.7 cases per 100,000 female population (compared to 4.0 per 100,000 population in Sarawak). In both states, the Malay population recorded a lower ASR compared to the Chinese population.

Comparing these against some countries in Cancer Incidence in Five Continents listings, we noted that the Sarawak Bidayuh population ranked among the highest in the world, closely matching China's Zhongshan and Zhuhai regions. Other places noted with a high incidence of NPC include Canada Nuvanut and USA Alaskan natives. This could be explained by shared hereditary risks. Natives in Borneo, as well as Alaskan regions were theorized to have shared origins in east Asia, with seafarers reaching Borneo (Hoh et al., 2022) and migrating through the Bering land bridge to Alaskan regions. More modern migration brought a sizeable population of Chinese to other regions, although the changes in cultural practices such as the consumption of preserved foods may differ. This is supported in part by the incidence rates from US Pacific Islands and the Chinese population in San Francisco Bay Area.

Limitations

As with other registry-based data (Izquierdo and Shoenbach, 2000; Thygesen and Ersbøll, 2014), this study had a few limitations. There was a lack of information regarding early symptoms and duration till diagnosis was established, as well as staging during diagnosis. Treatment and survival data was also incomplete.

In conclusion, Sarawak still has among the highest incidences of nasopharyngeal carcinoma in the world, particularly among the Bidayuh ethnicity. There is a need to increase health education efforts to increase awareness of cancers in general and to increase early screening to enable timely intervention.

Author Contribution Statement

HB, WYL and MW - Collection and preparation of data, primary descriptive statistics; WKY, NP, IY, OCH – Statistical analysis and writing of the text article. All authors had approved the final version of the manuscript.

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