# **Survival Rates of Cervical Cancer Patients in Malaysia**

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## Abstract

Cervical cancer is the most common malignant cancer of the female reproductive organs worldwide. Currently, cervical cancer can be prevented by vaccination and detected at an early stage via various screening methods. Malaysia, as a developing country faces a heavy disease burden of cervical cancer as it is the second most common cancer among Malaysian women. This population based study was carried out to fulfil the primary aim of determining the survival rates of Malaysian women with cervical cancer and associated factors. Data were obtained from two different sources namely, the Malaysian National Cancer Registry (MNCR) and National Health Informatics Centre (NHIC) from 1st January 2000 to 31st December 2005. Kaplan Meier analyses were conducted to identify the overall survival rates and median survival time. Differences in survival among different ethnic and age group were compared using the log-rank test. A total of 5,859 patients were included. The median survival time for cervical cancer in this study was 65.8 months and the 5-year survival rate was 71.1% . The overall observed survival rates at 1, 3 and 5 years were 94.1%, 79.3% and 71.1% respectively. The log-rank test finding also showed that there were significant differences in the 5-year survival rate among different ethnic groups. Malays had the lowest survival rate of 59.2% followed by Indians (69.5%) and Chinese (73.8%). The overall 5-year survival rate among patients with cervical cancer in Malaysia is relatively good. Age and ethnic groups remain as significant determining factors for cervical cancer survival rate.

Keywords: Cervical cancer - survival rate - ethnic group - Malaysia

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## Introduction

Cervical cancer is the most common malignant cancer of the female reproductive organ worldwide (Ishioka et al., 2006; Haghshenas et al., 2013). The estimated global annual incidence is 500,000 new cases and 300,000 deaths from which 80-85% of cases occur in developing and poor countries (Balkin, 2007; Ferlay et al., 2010; Maranga et al., 2013). Women in their perimenopausal years are at high risk and the peak incidence occurs mostly between age 50 (Balkin, 2007) and 52 (Cheung et al., 2011). Two most common types of cervical cancer are squamous cell carcinoma (74.4%) and adenocarcinoma (15.5%) (Brinton et al., 1987; Vizcaino et al., 2000; Romus et al., 2013).

There are several aetiological factors for cervical cancer and the most significant is due to persistent infection of specific human papillomavirus (HPV) strains, particularly type 16 and 18 which are the most common (Domingo et al., 2008; Haghshenas et al., 2013). Since HPV is a type of virus that is transmitted sexually (Shepherd et al., 2000), other known risk factors for cervical cancer are mostly related to sexual behaviour. These include the use of condom during coitus, the number of sexual partners and an early age of first intercourse (Shepherd et al., 2000; Hartmann et al., 2002; Fish, 2009; Vesco et al., 2011). Cigarette smoking is the only non-sexual risk factor for cervical cancer (Hartmann et al., 2002) and is clearly associated with increased risk of squamous cell carcinoma. Studies have shown increased risk of 50-60 percent for squamous cell carcinoma in current smokers (Vesco et al., 2011). This behaviour is consistently and strongly reported to be an important co-factor increasing risk by two- to fourfold (Hartmann et al., 2002).

The alarming statistics drive medical practitioners around the world trying to develop and implement various preventive strategies and treatment protocols. Currently, cervical cancer can be prevented by HPV vaccination and detected early through various screening methods: Papanicolaou smears (Pap smears), HPV-DNA testing and visual inspection (Balkin, 2007; Fernandez et al., 2014). It has been estimated that cervical screening prevents at least 70% of cases that could occur without screening (Sasieni et al., 2003; Howell-Jones et al., 2010). Early screening and detection can dramatically improve outcome as the

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#### Nor Asiah Muhamad et al

earlier the cellular changes are detected, the more likely it is for patients to live a normal life with higher chances of survival (Balkin, 2007). Conversely, poor survival and low quality of life occur when the cancer is detected at later stages of the disease. The chances of survival for patients diagnosed with stage IA is nearly 100% compared to patients diagnosed with stage IVB who has chances of survival of only 20% (Kyrgiou and Shafi, 2010; Razak et al., 2013).

Survival rates of cervical cancer for each country differ throughout the world and they are commonly based on the country's development status. The five-year survival rate of a cervical cancer victim was recorded to be high in developed countries and this became lower in less developed countries. Among developed countries, United States of America (US), Germany and Spain have a five-year survival rate of more than 60% (Hartmann et al., 2002; American Cancer Society, 2011; National Cancer Institute, 2013) and the five-year survival rate in England and Wales are 67.4% (Cancer Research UK, 2014). Developing countries such as China and Thailand observed a five-year survival rate exceeding 50% (Hartmann et al., 2002; Sumitsawan et al., 2011; Xiang et al., 2011). In contrast, developing countries such as Gambia and Uganda have a five year survival rate of less than 25% (Hartmann et al., 2002; Sankaranarayanan et al., 2011).

The treatment approach of cervical cancer depends on the stage and tumour size, age of the patient and comorbidities (Balkin, 2007; Horn et al., 2007). Usually, the standard first line treatments used are radiation therapy (RT), surgery and adjuvant chemotherapy with RT (Balkin, 2007; Ferlay et al., 2010). Treatment methods of early stages of cervical cancer are either RT and/or radical surgery since both are equally effective (Ferlay et al., 2010). Treatment for late and more advanced cervical cancer stages is surgery, radiation or both combined with chemotherapy (Ferlay et al., 2010; Samant et al., 2010; American Cancer Society, 2013a). Currently, concurrent chemotherapy plus radiotherapy (CCRT; concurrent chemoradiation) is the treatment of choice for locally advanced cervical cancer (Lee et al., 2010; Hsieh et al., 2013).

Consideration for conservative treatment is done only in early stages of the disease to preserve fertility. These include radical trachelectomy, cold knife conisation and simple trachelectomy with laparascopic lymphadenectomy (Karimi-Zarchi et al., 2013; Yousefi et al., 2013). They have been proven successful in preserving fertility for cervical cancer patients where those patients who received radical trachelectomy have become successfully pregnant and have good survival rates (Ishioka et al., 2006).

The burden of disease of cervical cancer in Malaysia, as a developing nation is high, being the second most common cancer and the fourth most common cause of death among Malaysian women (Maranga et al., 2013). The overall incidence rate of cervical cancer in Malaysia is 19.7 per 100,000 women. Chinese have the highest age-standardized rate (ASR) of 28.8 per 100,000 followed by Indians, 22.4 and Malays 10.5 per 100,000 women (Maranga et al., 2013).

**3068** Asian Pacific Journal of Cancer Prevention, Vol 16, 2015

Hence, this study was carried out to fulfil the primary aim in determining the survival rates of Malaysian woman with cervical cancer and factors associated with them.

## **Materials and Methods**

#### Data management

The detail of this study was described elsewhere (Abdullah et al., 2013a). A registry data was screened for both breast and cervical cancer patients from 1st January 2000 to 31st December 2005. Data were obtained from two different sources namely, the Malaysian National Cancer Registry (MNCR) and National Health Informatics Centre (NHIC). All patients diagnosed with cervical cancer with complete information were included in this study. Patients with missing information or incomplete data entries in the MNCR and NHIC such as date of diagnosis, date of remission or any other information on socio-demography were excluded. The status of the patients either dead or alive at the end of the study period and the time of death were obtained by examining the mortality data from the National Registration Department. From these, a new dataset was developed containing all the information of the patients.

A total of 12,299 patients from both government and private hospitals were identified. Of these, 5,859 patients were included in a single database.

#### Statistical analysis

Statistical analyses were performed using STATA version 11.2. Descriptive statistics were presented for patient characteristics. Kaplan Meier analysis was conducted to identify the overall survival rates and median survival time of the patients. Differences in survival among different ethnic and age groups were compared by using Log-rank test. The determination of associated factors to cervical cancer was done by using Multiple Cox Regression analysis. Two-tailed t-test with p-value of less than 0.05 was considered as statistically significant.

## **Results**

12,299 patients' records were retrieved and 5,859 (47.6%) patients with complete information were included in the study. 1,247 (21.3%) cases were certified dead due to the complications of cervical cancer and the remaining 4,612 cases (78.7%) were lost to follow-up or still alive by the end of the study period.

Patients' average age was 51 years old (SD 13.14). 65.6% were in the 45 years old or higher age group. More than half of the patients were Chinese (56.3%), followed by Malays (24.0%) and Indians (7.2%). Other ethnic group accounted for 12.5% as shown in Table 1.

The 1, 3 and 5 years survival rates by age at diagnosis and ethnicity were presented in Table 2. The median survival time was 65.8 months and the 5-year survival rate was 71.1% as shown by Kaplan Meier curve in Figure 1. The overall observed survival rates at 1, 3 and 5 years were 94.1%, 79.3% and 71.1% respectively. There were significant differences in survival rates between patients from different age groups when tested by using the logrank test. Women less than 45 years old have a better 5-year survival rate compared to those 45 years old and above (85.2 vs 63.8%) as shown in Figure 2. Similarly, women aged less than 45 years old had higher median survival months compared to women aged 45 years old and above (75.0 vs 64.5 months). There were significant differences of the 5-year survival rate among different ethnic groups (Figure 3). The Malays have the lowest survival rate at 59.2% followed by Indians (69.5%) and Chinese (73.8%). However, the median survival rate was about 65 months among all the 3 ethnicities.

The multiple cox regression analysis revealed that, age group and ethnicity were the associated factors to the survival of cervical cancer patients. Patients aged 45 years

 Table 1. The Characteristics of Cervical Cancer

 Patients in Malaysia

Characteristics		No. of cases (N=5859)	(%)
Ethnic	Malay	1409	24
	Chinese	3299	56.3
	Indian	420	7.2
	Other Malaysia	n 731	12.5
Age (years old)	Less than 45	2015	34.4
	At least 45	3844	65.6

Table 2. The Survival Rate of Cervical Cancer Patientsby Selected Factors

Factors		Survival Rates			
		1 year	3 years	5 years	
Age at diagnosis	< 45 years old	97.4	89.1	85.2	
	$\geq$ 45 years old	92.3	74	63.8	
Ethnicity	Malay	89.6	69.8	59.2	
	Chinese	95.5	82.4	73.8	
	Indian	93.1	75.8	69.5	



Figure 1. Kaplan Meier Overall Survival Estimates among Cervical Cancer Patients in Malaysia



Figure 2. Kaplan Meier Survival Estimates by Age Group among Cervical Cancer Patients in Malaysia



Figure 3. Kaplan Meier Survival Estimates by Ethnicity among Cervical Cancer Patients in Malaysia

Table 3. Hazard Ratio Associated Factors of CervicalCancer in Malaysia

Variables	Regression coefficient (b)	Hazard ratio (HR)	95%CI	p-value
Age group (	years old)			
<45 (ref)	0	1		
≥45	0.98	2.67	2.30, 3.09	< 0.001
Ethnicity				
Malay (ref)	0	1		
Chinese	-0.61	0.54	0.48, 0.61	< 0.001
Indian	-0.39	0.68	0.55, 0.84	< 0.001
Others	-0.84	0.43	0.34, 0.55	<0.001

old and above are 2.7 times more likely to die compared to those aged less than 45 years old. In terms of ethnicity, when compared to the ethnic Malays, the Chinese had 46% less chances of dying and Indians 32% (Table 3).

## Discussion

From the literature search, this study of survival rate among cervical cancer patients in Malaysia was the first study to collate data collected from the entire country. The strength of this study is the analysis of data collected nationwide by using and combining three national databases namely the Malaysia National Cancer Registry (MNCR), the National Health Informatics Centre (NHIC) and the National Registration Department. It encompasses all government and private hospital cases, districts and social classes, therefore showing the true magnitude of the disease's impact in Malaysia.

The survival of cervical cancer patients and indirectly, the prognosis of the disease depend on a few independent variables. The major factors are; stage, size and histopathology of the cancer. The minor factors include; the availability of effective prevention and treatment methods and socio-demographic factors such as age, ethnicity and sociocultural parameters.

Cervical cancer stages are determined by the International Federation of Gynaecology and Obstetrics (FIGO) staging system which categorised the cancer into stages according to tumour size. FIGO staging system has been the standard method in measuring survival rates of patients by cancer stages where the higher the cancer stage, the lower the survival rate (American Cancer Society, 2013b). For the histopathology factor, Chen et al., (2012)

#### Nor Asiah Muhamad et al

reported that they observed differences in survival rate of cervical cancer patients with different histopathology types (squamous cell carcinoma and adenocarcinoma). Those with squamous cell carcinomas were reported to have higher survival rates compared to patients with adenocarcinomas (66% and 63% respectively) (Chen et al., 2012).

Both developed and developing countries have effective empirical prevention and treatment methods and reflectively showed high cervical cancer overall survival rate. However, most of the less developed countries have poor survival rates. This study found that the overall Malaysian 5-year survival rate was 71.1% which can be considered very high compared to other countries, especially if compared among developing countries in Asia. It was reported that China (Kyrgiou and Shafi, 2010) and Thailand (American Cancer Society, 2011) have their overall survival rate of more than 50%. Other Asian countries such as Hong Kong, Singapore and South Korea have their overall survival rate higher than 65% (National Cancer Institute, 2013). Our findings also showed that Malaysian overall survival rate is at par with other developed countries such as France which has the overall survival rate of cervical cancer at 70% as reported by Brun et al., (2003). Other developed countries such as the United States, Australia and Japan have their 5-year survival rate at 73.3%, 73.6, and 71.5% respectively (Romus et al., 2013).

Similar to our finding, a recent study conducted in Hong Kong reported that the country also had a high overall survival rate of 71.3% among their cervical cancer patients (Romus et al., 2013). The high percentage of overall survival rate both in Malaysia and Hong Kong were most probably due to the extensive screening programmes, improvement of hospital equipment, new approach methods and readily available and accessible treatment methods for cervical cancer patients.

In contrast with the high survival rate in this study, which is 71.1%, a recent local study done by Razak et al., (2013) reported the overall 5-year survival rate of cervical cancer was only 39.7%. The contrary finding was due to the small sample size and characteristic. In their study, only 120 patients which were admitted to Hospital Universiti Sains Malaysia (HUSM), the referral centre of cervical cancer patients for the East Coast region of Peninsular Malaysia were selected. Furthermore, their sample represented only one government hospital where their study cohort covered only a specific region of Malaysia. In addition, their finding could only represent the Malay ethnic group since the Malays represented a large proportion of ethnicities in that region which incidentally, does not

In this study, out of 5,859 patients - 56.3% are Chinese, 24% Malays and 7.2% Indians. The highest frequency of cervical cancer cases in Malaysia was among the Chinese which is consistent with a study done by Domingo et al., (2008). Chinese women led the other races for the 5-year survival rate, with the highest survival rate of 73.8% despite them having the highest incidence rate of the cancer. The survival rate was relatively good among the Indians at 69.5% but the Malays have the lowest survival rate of 59.2%.

In spite of the high survival rate of cervical cancer patients in this study, many past studies have quoted that the general population of Malaysia lacks the general knowledge of cervical cancer. For instance, many respondents from a study by Wong et al., (2008) did not even know what the risk factors of cervical cancer are. Many of them also did not know important facts about cervical cancer; that this type of cancer is preventable through continuous screening, the early stages are asymptomatic and unmarried, non-sexually active individuals are also at risk for cervical cancer (Wong et al., 2008). The Malaysian population also tend to neglect the importance of cervical cancer screening even among the highly educated (Lim, 2003). Studies have shown that all cervical cancer patients that died due to the cancer do not undergo Pap smear in the past five years (Adeeb et al., 2008). These studies also added that Malaysians have the attitude to give up on their life if diagnosed with cancer since they strongly believe that death is inevitable and there is no cure for cancer.

The possible reason why the Malays ended up with the lowest 5-year survival rate is mainly because they tend to have peculiar health seeking behaviour, where they have a strong belief in traditional treatment rather than modern treatment. They will continue seeking traditional treatment despite having a modern rural health service (Ariff and Beng, 2006). It is also noted that Malays tend to seek treatment at a later stage of the cancer and presented with large tumours (Wong et al., 2009; Abdullah et al., 2013b). This behaviour was also observed among Malay patients with breast cancer (Hisham and Yip, 2004).

Malaysia Cancer Statistics (2007) reported that the cervical cancer incidence rate increases with age after 30 years old and the incidence peak at the age of 65-69 (Omar and Ibrahim Tamim, 2011). Brun et al., (2003) reported that the patient's age, one of the minor risk factor, play an important role in cervical cancer survival. This study showed that about 65% of individuals were between 45 years old and above. The mean age at diagnosis was 51 years old. It also showed that patients aged below 45 years old have a better 5-year survival compared to those aged 45 years and above.

The high survival rate of cervical cancer found in this study speaks for the effectiveness of the awareness campaigns done in Malaysia. Government and non-profit organizations in Malaysia have played a very important role in the survival of cervical cancer patients. Both the Ministry of Health Malaysia (MOH) and non-profit organizations (such as Malaysian Medical Association and National Cancer Council) have carried out several cervical cancer awareness campaigns (Cheah and Looi, 1999; Lim, 2002; Lim, 2006). There have been many similar campaigns done in recent years which most likely contributed to the high 5-year survival rate in our study. Among the recent cervical cancer campaigns done are; The Cervical Cancer Awareness and Health Campaign (2009), organised by Universiti Tunku Abdul Rahman (UTAR), Crisis Relief Squad of the MCA Foundation (Yayasan CRSM), and the Obstetrical and Gynaecological Society of Malaysia and, Cervical Cancer Awareness & HPV

Vaccination Campaign (2011) which was organized by the International Islamic University of Malaysia (IIUM) Health & Wellness Centre with joint effort from Glaxo Smith Kline (GSK). The most recent one is "MAY Cares For You" Campaign (2013). This campaign was done in collaboration with May, the beauty soap and shower cream brand from Lam Soon Edible Oils Sdn Bhd and the National Cancer Society of Malaysia (NCSM).

Although this study showed a high survival rate for cervical cancer patients in Malaysia, it lacked in some important data that can determine much more accurately, the survival of cervical cancer patients. The missing data in this study are; type of cervical cancer and histopathology diagnosis (either squamous cell carcinoma or adenocarcinoma), stages of the cancer for each patient and treatment methods received by these patients. Nevertheless, this study still has described some of the important data and information which can be used by other cervical cancer researches in the future.

In conclusion, the overall 5-year survival rate among patients with cervical cancer in Malaysia is relatively good as compared to developed nations. However it is low in Malays as compared to other ethnic groups. Age and ethnic groups remain significant determining factors of cervical cancer survival rate. It is recommended that the cancer registry should be updated and obtains more details on other risk factors such as the stage of the disease, type of cervical cancer and mode of treatments for case registry completeness.

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Nor Asiah Muhamad et al

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