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BRIEF REPORT

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Clinical features of cervical cancer at a national cancer center in Phnom Penh, Cambodia: A descriptive cross-sectional study

Aya Tanaka[1], Linka Koun[2], Rei Haruyama[1,*], Kyna Uy[2], Maryan Chhit[2], Lumpiny Kim[2], Noriko Fujita[1], Yutaka Osuga[3], Tadashi Kimura[4], Kanal Koum[5]

[1] Bureau of International Health Cooperation, National Center for Global Health and Medicine, Tokyo, Japan;
[2] Department of Obstetrics and Gynecology, Khmer-Soviet Friendship Hospital, Phnom Penh, Cambodia;
[3] Department of Obstetrics and Gynecology, Faculty of Medicine, The University of Tokyo, Tokyo, Japan;
[4] Department of Obstetrics and Gynecology, Osaka University Graduate School of Medicine, Osaka, Japan;
[5] Cambodian Society of Gynecology and Obstetrics, Phnom Penh, Cambodia.

Abstract: The clinical features of newly diagnosed cervical cancer in Cambodia are poorly documented. We aimed to describe the histologic type and stage distributions of newly diagnosed cervical cancer patients at the Khmer Soviet Friendship Hospital in Phnom Penh, which is one of the two national cancer centers in Cambodia. A descriptive cross-sectional study was conducted using the Gynecologic Test Registry of the gynecology department between January and December 2019. In 2019, 351 women were histologically diagnosed with cervical cancer, representing approximately one-third of the estimated total cases occurring in the country. The mean age at presentation was 54.7 years. The histologic type distribution was largely consistent with other Asian countries, with squamous cell carcinoma accounting for 83.8%, followed by adenocarcinoma (15.4%). Among 309 patients with recorded staging information, 57.6% were advanced-stage cancers (*i.e.* stage IIB or higher). Raising awareness of early symptoms of cervical cancer, increasing access to cancer diagnosis, and better recording of patients' clinical information are important to improve cervical cancer management in Cambodia.

***Keywords*:** uterine cervical neoplasms, delayed diagnosis, neoplasms by histologic type, Cambodia

Introduction

Cervical cancer is caused by persistent infection with oncogenic human papillomavirus (HPV), which progresses slowly from precancerous lesions to invasive carcinoma (*1*). If detected at an early stage of progression, it is more likely treatable with good survival prognosis (*2*). However, in countries without effective cervical cancer screening and early diagnosis programs, patients are often diagnosed as advanced-stage cancer with high mortality.

In Cambodia, cervical cancer is one of the leading cancers in women with an estimated 1,100 new cases and 600 deaths in 2020 (*3*). These numbers correspond to an age-standardized incidence rate of 14.0 per 100,000 and mortality rate of 8.3 per 100,000, both of which are higher than global estimates. The Cambodian Ministry of Health has placed cervical cancer as one of its priorities for non-communicable disease agenda, and vaginal inspection-based screening is offered to women in some health centers and hospitals (*4*). However, the screening test is not yet freely available and widely recognized by many women. In a 2016 population-based survey, the percentage of women aged 18–69 years who have ever had cervical cancer screening was only 11.3% (*5*). Often, women visit health facilities only when they have recurring symptoms of abnormal vaginal bleeding. The exact number of women affected with the cancer and their clinical features, including stage at diagnosis, remain unknown due to a lack of cancer registration system. Previous studies on cervical cancer in Cambodia are limited to those on cancer awareness and the prevalence of HPV and cervical dysplasia (*6-9*).

The Khmer-Soviet Friendship Hospital (KSFH) is a national cancer center located in Phnom Penh, the capital city of Cambodia. It is one of four public hospitals with pathology services and one of two with cancer treatment capacity. Women suspected of having cervical cancer are referred to a gynecology department across the country. In this study, we aimed to describe the histologic type and stage distributions of newly diagnosed cervical cancer patients presenting at the KSFH.

Materials and Methods

Study design and sample

This descriptive cross-sectional study was conducted using the Gynecologic Test Registry of the gynecology out-patient department of the KSFH between January and December 2019, before the COVID-19 pandemic. This registry compiled information on patients who underwent gynecological tests, such as cytology, colposcopy, and biopsy. In addition to patient name, identification number, age, parity, place of residence, and type of test received, the registry also included test results, clinical diagnosis, and stage at diagnosis for malignant cases. For cervical cancer patients, staging was recorded using the 2009 International Federation of Gynecology and Obstetrics (FIGO) staging system (*10*). We extracted data of histologically confirmed cervical cancer patients for this study.

Data analysis

Descriptive statistics were performed to examine the sociodemographic and clinical characteristics of the study participants. As in previous studies, we defined FIGO stage IA to IIA patients as early-stage cancer, and FIGO stage IIB or higher as advanced-stage cancer (*11-14*). At the KSFH, early-stage cancers are usually operated surgically with or without adjuvant external beam radiotherapy and chemotherapy (brachytherapy is being planned for installation, but not yet available). Excluding cases with missing staging information, univariate logistic regression analysis was performed to examine factors associated with advanced-stage presentation. Data analysis was performed using Stata/SE 16.1 (Stata Corporation, College Station, TX, USA). Statistical significance was set at $p \leq 0.05$. Ethical approval was obtained from the Cambodia National Ethics Committee for Health (312 NECHR) and Ethics Committee of the National Center for Global Health and Medicine in Japan (NCGM-G-004021-00). Since the study used an existing database, informed consent was substituted by making research information widely available and ensuring that women had the opportunity to opt out of the study.

Results and Discussion

A total of 351 histologically confirmed cervical cancer patients were analyzed in this study (Table 1). The mean age at presentation was 54.7 ± 9.6 years, ranging between 30–81 years. Women presented from across the country, with 28.8% from Phnom Penh or Kandal (*i.e.*, a province surrounding Phnom Penh), 35.9% from the five adjacent provinces of Kandal, and the remaining 17 distant provinces located over 3–10 h drive to Phnom Penh. All the patients underwent cervical biopsy, and pathological results were recorded. Squamous cell carcinoma (SCC) accounted for 83.8% of the cases, followed by adenocarcinoma (15.4%), small cell carcinoma (0.6%), and undifferentiated carcinoma (0.3%). Staging information was recorded for 309 patients (88.0%). Among them, 57.6% were advanced-stage cancers (Table 2). The proportions of advanced-stage cancer were high in women who were aged 30–39 years (68.4%), over 70 years (65.2%), had 1–3 children (61.2%), or lived in adjacent provinces of Kandal (61.4%); however, no statistically significant association was observed.

This study examined the histologic type and stage distributions of newly diagnosed cervical cancer patients that presented to the KSFH in 2019. Although this was a single-center analysis, it is the first to describe the clinical features of cervical cancer at a national cancer center in Cambodia. Overall, there were 351 patients, representing approximately one-third of the estimated total cases occurring in the country (*3*). Cervical cancer was more commonly diagnosed among

Table 1. Sociodemographic and clinical characteristics of the study sample

Characteristics	*n* (%)
Total	351
Age, years	.
Mean	54.7 ± 9.6
30–39	20 (5.7)
40–49	77 (21.9)
50–59	148 (42.2)
60–69	80 (22.8)
≥ 70	26 (7.4)
Parity	
0	30 (8.6)
0–3	136 (38.8)
≥ 4	181 (51.6)
Not reported	4 (1.1)
Place of residence	
Phnom Penh or Kandal	101 (28.8)
Adjacent province of Kandal†	126 (35.9)
Distant province	124 (35.3)
Histopathology result of cervical biopsy	
Squamous cell carcinoma	294 (83.8)
Adenocarcinoma	54 (15.4)
Small cell carcinoma	2 (0.6)
Undifferentiated carcinoma	1 (0.3)
Stage at diagnosis	
I	
IA	2 (0.6)
IB	48 (13.7)
II	
IIA	81 (23.1)
IIB	78 (22.2)
Unknown subclassification	1 (0.3)
III	
IIIA	38 (10.8)
IIIB	44 (12.5)
Unknown subclassification	6 (1.7)
IV	
IVA	3 (0.9)
IVB	1 (0.3)
Unknown subclassification	7 (2.0)
Unknown stage	42 (12.0)

†Prey Veng, Kampong Cham, Kampong Chhnang, Kampong Speu, or Takeo

Table 2. Advanced-stage presentation and its associated factors

Characteristics	Advanced-stage presentation		Crude odds ratio (95% CI)	*p* value
	Yes *n* (%)	No *n* (%)		
Total	178 (57.6)	131 (42.4)		
Age				
30–39	13 (68.4)	6 (31.6)	1.5 (0.5–4.1)	0.5
40–49	40 (58.8)	28 (41.2)	1.0 (0.5–1.8)	0.9
50–59	78 (59.5)	53 (40.5)	1	NA
60–69	32 (47.1)	36 (52.9)	0.6 (0.3–1.1)	0.1
≥ 70	15 (65.2)	8 (34.8)	1.3 (0.5–3.2)	0.6
Parity				
0	12 (44.4)	15 (55.6)	1	NA
1–3	74 (61.2)	47 (38.8)	2.0 (0.8–4.6)	0.1
≥ 4	90 (57.0)	68 (43.0)	1.7 (0.7–3.8)	0.2
Not reported	2 (66.7)	1 (33.3)	2.5 (0.2–31.0)	0.5
Place of residence				
Phnom Penh or Kandal	51 (58.0)	37 (42.0)	1	NA
Adjacent province of Kandal[†]	70 (61.4)	44 (38.6)	1.2 (0.7–2.0)	0.6
Distant province	57 (53.3)	50 (46.7)	0.8 (0.5–1.5)	0.5
Histologic type				
Squamous cell carcinoma	150 (58.4)	107 (41.6)	1	NA
Non-squamous cell carcinoma	28 (53.9)	24 (46.1)	0.8 (0.5–1.5)	0.5

[†]Prey Veng, Kampong Cham, Kampong Chhnang, Kampong Speu, or Takeo. CI: confidence interval

women in their 50s. Histologically, SCC accounted for 83.8% of the cases, followed by adenocarcinoma (15.4%). Among patients with recorded staging information, 57.6% were in their advanced stage (*i.e.*, stage IIB or higher).

Cervical biopsy and pathological examination are necessary to establish a definitive diagnosis of cancer and identify the histologic type (*15*). This analysis confirmed that all suspected and clinically diagnosed cervical cancer patients underwent biopsy at the KSFH. The proportion of SCC was largely consistent with studies from Thailand (71.1%), China (74.5%), and Japan (72.6%) (*16-18*).

The proportion of advanced-stage cancer (*i.e.*, stage IIB or higher) was unexpectedly lower than that in studies conducted in similar settings of lower-middle income countries. The advanced-stage cervical cancer presentation was reported to be 64% of 202 patients at a referral hospital in Tanzania, 78% of 246 at a regional cancer center in India, and 81% of 110 at two referral hospitals in Nepal (*11,13,14*). This may be due to successful early referrals of suspected cervical cancer patients from district hospitals and non-governmental organization clinics to the KSFH. However, this may also be because many of the patients we excluded due to missing information on staging (12% of 351 patients) may be advanced-stage cancers. The KSFH is a public hospital that serves many patients with low socioeconomic status, and some women refuse to get tested and treated due to fear of procedures and high healthcare costs. Pelvic examination, transvaginal ultrasound, and renal ultrasound are usually performed; however, computed tomography and magnetic resonance imaging are rare (< 10%), thereby limiting the evaluation of lymph nodes, local extension, and systemic spread.

A systematic review of 25 studies examining the determinants of advanced-stage presentation found that women with no formal education and those residing in rural areas were significantly more likely to present in the advanced stage than their counterparts (*19*). However, in our study, these factors showed no association. Lack of association with place of residence was contrary to our expectation, because public hospitals with pathology laboratories are only located in Phnom Penh and patients have to visit one of these hospitals themselves, including the KSFH, for a biopsy and pathological examination. An explanation may be that women suspected of having advanced-stage cervical cancer but living in rural provinces may be unable to reach the KSFH for definitive diagnosis and treatment. In contrast, women suspected of having early-stage cervical cancer and living in Phnom Penh and Kandal may visit other hospitals from the outset, including those in neighboring countries, such as Thailand, Singapore, and Vietnam.

This study utilized a clinical registry introduced through a cervical cancer prevention and control project by professional societies in Cambodia and Japan (*20*). It contained minimum possible information of all patients receiving gynecologic tests at the KSFH. Although we examined the clinical features of newly diagnosed cervical cancer patients presenting at a national cancer center for the first time, there are several limitations. First, data on patients' education, occupation, household income, comorbidity, and history of screening were not available in the registry, and we could not fully examine the baseline characteristics of the patients, as well as the adjusted effect of these factors on advanced-stage presentation. Second, we were unable to identify whether the patients underwent any treatment because this information was not included in the registry,

and individual medical records do not exist at the gynecology department of KSFH. We attempted to go through the surgical records and pathology results of surgical specimens for early-stage patients, but we found that personal identification numbers are often incorrectly recorded, or two or more numbers exist for one person. It was also difficult to identify patients who underwent radiotherapy or chemotherapy at the oncology department or those who were referred elsewhere. It is critical to improve the recording of each patient's clinical information to better understand the current situation in the management of cervical cancer and formulate strategies to reduce preventable deaths. This will become even more important with the government's recent move to scale-up cervical cancer screening, as screen-detected invasive cancer will surely increase in previously unscreened large populations (*2,21*).

In conclusion, our study showed that over half of women presented at an advanced stage. Raising awareness of early symptoms of cervical cancer, increasing access to cancer diagnosis, and better recording of patients' clinical information are important to improve cervical cancer management in Cambodia.

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Address correspondence to:
Rei Haruyama, Bureau of International Health Cooperation, National Center for Global Health and Medicine, 1-21-1 Toyama, Shinjuku-ku, Tokyo 162-8655, Japan.
E-mail: rharuyama@it.ncgm.go.jp