

### Epidemiological characteristics of cervical cancer in a tertiary care hospital, western Saudi Arabia. A retrospective record-based analysis from 2002-2018

Fayssal M. Farahat, MD, PhD, Norah T. Faqih, Medical Student,  
Razan S. Alharbi, MBBS, Raheed I. Mudarris, MBBS,  
Sahl A. Alshaiikh, Medical Student,  
Hatim M. Al-Jifree, MB, ChB, FRCSC.

#### ABSTRACT

**Objectives:** To investigate the epidemiological characteristics of cervical cancer cases reported at a tertiary care teaching hospital in western Saudi Arabia.

**Methods:** A retrospective chart review was conducted on medical records of patients diagnosed with cervical cancer at King Abdulaziz Medical City, Jeddah, Saudi Arabia. Data were collected on demographic characteristics, histological types and stage, treatment modalities, and disease outcomes.

**Results:** Cervical cancer was diagnosed among 89 patients from 2002 to 2018. History of pap smear was reported among 31 cases (34.8%). Squamous cell carcinoma was the most common reported histopathological subtype. Almost one third (29.2%) of the patients were at stage III or IV at the time of diagnosis. The most frequent treatment regimen was combined radio/chemotherapy. Kaplan-Meier analysis showed an overall survival rate of 81.5%.

**Conclusion:** The lack of an effective screening program for cervical cancer increases the likelihood of a late diagnosis and higher rates of complications and mortality. Public health programs should focus on cancer screening, screening, and reporting HPV infections, and supporting HPV vaccination activities.

**Keywords:** cervical cancer, incidence, human papillomavirus, elimination

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Worldwide, among women, cervical cancer ranks 4th after breast, colorectal, and lung cancer. A global study estimated an occurrence of 570,000 cases of cervical cancer and 311,000 related deaths in 2018.<sup>1</sup> Another study in 2015 reported 527,000 cases and 265,000 deaths.<sup>2</sup> In Saudi Arabia, cervical cancer ranks the 9th most common form of cancer among females

aged 15 to 44 years.<sup>3</sup> Human papillomavirus (HPV) is a sexually transmitted virus that has been identified as the main cause associated with the occurrence of cervical cancer.<sup>4</sup> Torre et al<sup>2</sup> identified a prevalence of HPV infection in the young population ranging from 5% to 21%, depending on the geographic location. The highest percentages were recorded in developing countries. It has been concluded that HPV carries a burden on almost a third of the communities worldwide.<sup>5,2</sup> Human papillomavirus has several genotypes, some of which are mainly responsible for the genital warts, namely genotypes 6 and 11. In contrast, the high-risk genotypes 16 and 18 are responsible for approximately 70% of all cervical cancers.<sup>4</sup> After an infection, HPV goes into an asymptomatic phase or a subclinical phase where the symptoms are too minor to be assessed. This phase is followed by a neoplasm phase, in which it can develop into either a wart or a malignant lump (especially in women's cervix), depending on the virulence of the strain itself.<sup>6</sup> Cervical cancer is considered a preventable tumor, where primary prevention through HPV vaccination and screening programs can play a significant role in eliminating cervical cancer worldwide.<sup>7</sup> The World Health Organization (WHO) emphasized the need to establish a high-quality surveillance and monitoring system for non-communicable diseases, including cervical cancer, as an essential measure to identify the magnitude of the problem and effectively reduce the burden associated with such conditions.<sup>4</sup>

Epidemiological data on cervical cancer and the associated burden in Saudi Arabia are still insufficient. Thus, this study aimed to investigate the epidemiological characteristics of cervical cancer cases diagnosed at King Abdulaziz Medical City in western Saudi Arabia.

**Methods.** A descriptive retrospective record-based analysis of a series of cervical cancer cases was conducted at King Abdulaziz Medical City, Ministry of National Guard-Health Affairs, Jeddah, Saudi Arabia. This tertiary care teaching hospital serves the National Guard military personnel, employees, and their families. It includes the Princess Noorah Oncology Center that provides care to patients with cancer and blood disorders in the western region of Saudi Arabia.

The study was conducted between June and July 2019. Medical records of patients with documented clinical diagnosis of cervical cancer since 2002 were included. Data were collected on demographic characteristics, body mass index (BMI), associated comorbidities, including sexually-transmitted infections (STIs), tumor histological type and stage, in addition to treatment modalities and disease outcome.

The study was approved by the Institutional Review Board (IRB) office of King Abdullah International Medical Research Center (KAIMRC) (IRBC/1075/19). The study was conducted according to principles of Helsinki Declaration.

**Statistical analysis.** Data were analyzed using the IBM SPSS Statistics for Macintosh, version 25 (IBM Corp, Armonk, NY). The Fisher's exact test was used to examine differences in categorical variables. Survival analysis was performed using the Kaplan-Meier method. The log-rank test was used to evaluate statistically significant differences. Overall survival was calculated from the date of reported diagnosis to the time of death or the last follow-up visit. Two-sided  $p < 0.05$  was considered statistically significant.

**Results.** A total of 89 patients were clinically diagnosed with cervical cancer from 2002 to 2018. Most of the cases were reported from 2014-2018 ( $n=53$ , 59.6%). The mean $\pm$ SD age of the patients at the time of diagnosis was  $56.9 \pm 13.0$  and ranged from 31-90 years. The majority of the patients were Saudi (89.9%). Of the total number of patients, 71 were married, 13 widowed, and 5 divorced. More than half of the patients (53.9%) were obese. The mean $\pm$ SD BMI was  $30.9 \pm 8.7$ . Comorbidities among the studied patients included diabetes mellitus ( $n=28$ , 31.5%), cardiovascular disease ( $n=29$ , 33.7%), and renal problems ( $n=25$ , 29.2%).

History of pap smear was reported among 31 cases (34.8%) (Table 1). At the time of diagnosis, 7 patients were at Stage I (9.3%), 42 at Stage II (56.0%), 9 at Stage III (12.0%), and 17 at Stage IV (22.7%). During the study period, 10 patients died, and more than half of whom were at stage III or IV (Table 2).

Histopathological subtypes were available for 34 cases. The most common was squamous cell carcinoma ( $n=28$ , 82.4%), adenocarcinoma ( $n=4$ , 11.8%), small cell carcinoma ( $n=1$ , 2.9%), and undifferentiated carcinoma ( $n=1$ , 2.9%). There was one case diagnosed as squamous cell carcinoma in situ.

The most frequent treatment regimen used was radio-chemotherapy ( $n=37$ , 41.6%). The overall survival rate of the studied patients was 81.5%, and the overall median time to death was 48 months (Figure 1).

We also searched for documented diagnosis of genital warts during the last 5 years of the study from

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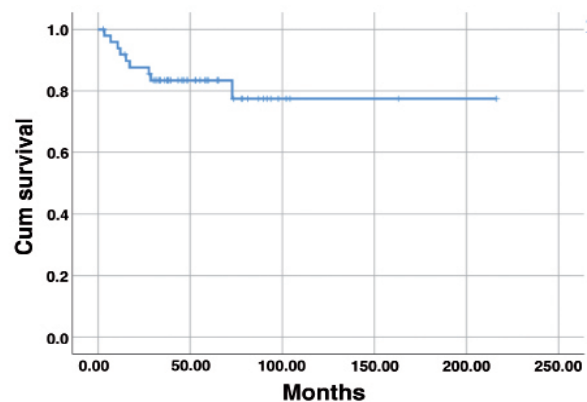
**Table 1** - Demographic and clinical characteristics of the studied patients.

Variable	n (%)
<i>Age (years)</i>	
≤55	47 (52.8)
>55	42 (47.2)
Mean (95%CI)	56.9 (54.1, 59.6)
<i>Nationality</i>	
Saudi	80 (89.9)
Non-Saudi	9 (10.1)
<i>Marital status</i>	
Married	71 (79.8)
Widowed	13 (14.6)
Divorced	5 (5.6)
<i>Body mass index</i>	
Normal	22 (24.7)
Overweight	19 (21.3)
Obese	48 (53.9)
Mean (95%CI)	30.8 (29.0, 32.6)
<i>History of comorbidities</i>	
Diabetes mellitus	28 (31.5)
Cardiovascular disease	30 (33.7)
Renal disease	26 (29.2)
<i>History of pap smear</i>	
Yes	31 (34.8)

**Table 1** - Number of patients and deaths distributed according to cancer stage at the time of diagnosis.

Stage	Number of death/ number of cases	Case fatality (%)
Stage I	0/7	0
Stage II	4/42	9.5
Stage III	2/9	22.2
Stage IV	4/17	23.5

Fisher's exact test:  $p=0.23$



**Figure 1** - Kaplan-Meier curve of overall survival.

2014-2018. This search aimed to estimate the burden of genital warts, which is the main risk factor for cervical cancer in the population. There were only 5 medical charts with documented clinical diagnosis of genital warts. Out of the 5 cases diagnosed with genital warts, 3 were females, none of whom had cervical cancer. In addition, no data were available on the type of HPV.

**Discussion.** The current study reported a relatively increasing number of cervical cancer cases over the last 5 years of the study, which may reflect the increased number of referrals to the oncology center at KAMC. However, the observed increasing number of cases over the years maybe alarming.

It was difficult based on the current single-center record-based study to estimate the incidence of cervical cancer, however, previous reports showed a low incidence in Saudi Arabia (3.5 per 100,000 women).<sup>3</sup> This estimate is lower than that of both developed countries (9.9 per 100,000 women) and developing countries (15.7 per 100,000 women).<sup>1</sup>

On the other hand, most cases are discovered at a late stage (Stage IIb, III, and IV). These observations emphasize the need to enhance cervical cancer screening programs and awareness campaigns for early detection of cases.

Overall survival rate of patients in this study was 81.5%. None of the Stage I patients died compared to 9.3% among Stage II and 23% among Stage III and Stage IV patients. Surgery and radiotherapy combination had the highest median survival (100 months or approximately 8 years). Most probably, those patients were diagnosed at an early stage. In contrast, chemotherapy is usually applied in advanced stages, and thus is associated with higher mortality. In previous studies, the 5-year overall survival rate among the Moroccan population was 63.2%;<sup>8</sup> however, it reached 67% among Canadians,<sup>9</sup> and 69.8% among British populations.<sup>10</sup> These survival rates are much higher than a study in Kenya where the 2-year overall survival rate was less than 20%. Late diagnosis has been associated with a lack of awareness on cervical cancer, lack of screening programs, delay in seeking medical advice, and delay in referral to appropriate healthcare service.<sup>8</sup>

In the current study, only one-third of the cases had a history of pap smear. Although cervical cancer screening has improved during the past few years, where gynecologists and family medicine physicians used to offer the pap smear testing to women who visit the clinics for contraceptive consultation/use, or other gynecological complaints, screening for cervical cancer is still not emphasized adequately for the high risk women,

and data on adherence to the screening programs are insufficient. Moreover, these screening tests depend on cytological analysis and no virological screening is being implemented. The lack of screening for cervical cancer and awareness among women increases the likelihood of a late diagnosis of the disease and hence the complications and higher rates of mortality.<sup>1</sup>

Regarding genital warts, the single-center experience of the current study may limit our ability to estimate the real burden; moreover, under-reporting of cases with genital warts seen by dermatologists or primary care physicians may be another contributing factor. However, the current findings of only 5 cases over a 4-year period are lower than a previous study by Madani<sup>11</sup> (2006), who reported an annual incidence of 1.4 genital wart cases per 100,000 population (approximately 200 cases are reported to the Ministry of Health [MOH] annually).

Saudi Arabia, similar to other countries in western Asia and northern Africa, has the lowest incidence of cervical cancer associated with a low prevalence of HPV. The rank of cervical cancer in these countries is more than 6 compared to all other cancer sites in women of all ages. The estimated low burden has been attributed to the sexual behavior in these communities with limited exposure to HPV infections.<sup>1</sup> However, continuous surveillance and emphasis on primary and secondary prevention are required to achieve elimination of cervical cancer in this region with high potential for success. Recently, the Saudi MOH has commenced HPV vaccination for young girls aged 11 to 12 years old—a vital step toward approaching the goal of cervical cancer elimination in the country. This pattern of providing the vaccine for those who are less than 15 years is considered less costly than getting vaccinated at an older age (above 15 years old) because of the fewer doses and follow-up visits required.<sup>12,13</sup> Additionally, proposing the vaccine to the general population as a safe and effective vaccine for the prevention against cancer cervix would impact their willingness to receive it.

**Study limitations.** The current study was limited because of the retrospective nature of data collection. There is a lack of information on socioeconomic characteristics, level of education, and sexual history, which have been previously discussed as risk factors associated with an increased incidence of cervical cancer.<sup>8</sup> Some other information was also missed related to the history of genital warts, pap smear, and history of previous hospital management. Estimates of survival analysis might be overestimated with the selection of patients with advanced conditions.

In conclusion, the current study is an overview of epidemiological characteristics of cervical cancer cases in Princess Noura Oncology Center, western Saudi Arabia. Late diagnosis increases the likelihood of poor outcome and mortality. In the meantime, cervical cancer has a potential for elimination in Saudi Arabia; however, public health programs should focus on cancer screening, screening and reporting HPV infections and supporting HPV vaccination activities. Awareness programs are always necessary and crucial toward the success of such interventions.

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*From the Infection Prevention and Control Department (Farahat), King Abdulaziz Medical City, Ministry of National Guard Health Affairs; from King Abdullah International Medical Research Center (Farahat, Al-Jifree); from the College of Medicine (Farahat, Alshaikh, Al-Jifree), King Saud bin Abdulaziz University for Health Sciences, Jeddah; from the College of Medicine (Faqih), Umm Al-Qura University, Makkah; from the College of Medicine (Alharbi, Mudarris), Ibn Sina National College; and from the Department of Oncology (Al-Jifree), King Abdulaziz Medical City, Ministry of National Guard Health Affairs, Jeddah, Kingdom of Saudi Arabia.*

*Address correspondence and reprints request to: Dr. Fayssal M. Farahat, Infection Prevention and Control Department, King Abdulaziz Medical City, Ministry of National Guard Health Affairs, Riyadh, Kingdom of Saudi Arabia. E-mail: fmfayssal@gmail.com  
OCID ID: <https://orcid.org/0000-0001-5186-2872>*

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