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Original Article


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Abstract

Background: Cervical cancer is the ninth most common female malignancy in the Gulf Cooperation Council (GCC) States. We describe trends in cervical cancer incidence among GCC nationals. GCC states include Bahrain, Kuwait, Oman, Saudi Arabia, Qatar and the United Arab Emirates; which share similar demographic, socioeconomic and cultural backgrounds.

Methods: The Gulf Centre for Cancer Control and Prevention (GCCCP) has maintained a database of cancer in the GCC states since 1998. Women diagnosed with invasive cervical cancer during the 15 years 1998–2012 were included (N=2,332). Age–specific incidence over three periods (1998–2002, 2003–2007 and 2008–2012) are presented for all states combined. Trends in the frequency of registered cases, age-standardized incidence rates (ASRs) and in the distribution of stage at diagnosis for the six member states are compared between the three periods.

Results: Over the 15–year period, the peak age of cervical cancer diagnosis has slightly shifted towards older age. While the number of cases in the GCC has increased, the ASR has decreased. 39% of women were diagnosed in localized stage. The proportion of unknown stage ranged between 10% in the UAE and 58% in Oman, and has increased over time in Kuwait, Oman and the UAE.

Conclusion: The present study indicates some success in cervical cancer preventive measures but the GCC may still see an increase in the number of cases in the coming years. More efforts should be directed towards documentation of stage and towards early diagnosis.

Keywords: Cervical cancer, Gulf Cooperation Council, Saudi Arabia, Kuwait, Qatar, Oman, United Arab Emirates, Bahrain, incidence, stage

Introduction

Cervical cancer is the fourth most common female malignancy world–wide, but its incidence varies widely between world regions, the highest being in Southern Africa and lowest in Western Asia.¹ This variation mainly reflects both the prevalence of high–risk human papilloma virus (HPV), which is the main risk factor for cervical cancer development, and the intensity of detection and removal of premalignant and in–situ intraepithelial lesions mainly by pap–tests. In countries that have introduced organized screening programs, incidence of invasive cervical cancer has drastically fallen since the 1930s and a decline in mortality followed in parallel.²,³ However, low– and middle–income countries (LMIC) have not benefitted equally from this decline and they now carry a disproportionately high burden of deaths due to cervical cancer.⁴ This is mainly because women in LMICs face barriers to access cervical cancer screening. If a woman eventually develops cervical cancer, inadequate access to treatment also results in lower survival and contributes to the higher mortality in these countries. Financial and other barriers to HPV vaccination are expected to widen the gap in cervical cancer burden between high–income and LMICs as vaccination is estimated to eventually prevent about 37% of cervical cancer cases if it reaches 70% coverage and theoretically 90% of cases with perfect use.⁵,⁶

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Cervical cancer is the 9th most common cancer in women of all ages among Gulf Cooperation Council (GCC) nationals, and the 5th most common in women aged 30–44 years. The GCC states (Saudi Arabia, United Arab Emirates, Oman, Kuwait, Bahrain and Qatar) share similar demographic, socioeconomic and cultural backgrounds. They are all classified by the United Nations Development Program (UNDP) as having a very high human development index. In 2011, the GCC had a total population of around 46 million, approximately half of which are citizens including almost 12 million females. The GCC states have been undergoing rapid demographic and cultural changes since the 1970s as well as changes in health services. These changes may affect lifestyle choices including smoking and reproductive patterns which in turn may affect cervical cancer incidence, age of occurrence and stage at diagnosis.

The World Health Organization recommends cervical screening at least once for every woman between age 30 and 49, and screening recommendations were published by the Saudi Ministry of Health in 2014. However, none of the GCC states have established screening program with the exception of the Emirate of Abu Dhabi in the UAE, which has started a cervical cancer screening program in 2012. Pap–testing in the GCC remains largely absent unless a woman requests it or the healthcare provider offers it to eligible women opportunistically when they present for other reasons. Therefore, despite cervical cancer incidence in the GCC being similar to that in countries with established screening programs, the lack of organized screening programs may lead to women being diagnosed at later stage. The UAE have also introduced HPV vaccination in their immunization schedule in 2008.

GCC member states all have population–based national cancer registries and cancer is a statutory notifiable disease. The Gulf Centre for Cancer Control and Prevention (GCCCP) maintains a database of cancer in the GCC states since 1998. This offers an opportunity to assess similarities and differences between GCC states. Including a 15–year period of population–based data and pooling GCC nationals together also enables examining age– and stage– specific incidence rates for countries with low incidence and a small population.

Monitoring trends in cancer incidence is crucial for planning services to meet future demands for diagnosis and treatment, and to assess the priorities for preventive measures including vaccination and screening. The aim of this study is to provide detailed trends in cervical cancer incidence among GCC nationals.

Methods

Incident cancer cases are registered in national registries of GCC states in a similar way by active case finding, where trained registrars search hospital pathology reports for histologically confirmed malignancies; this is complemented by other sources like death notifications, out–patient records and radiology. The GCCCP receives all data on malignant neoplasms yearly from the national registries and data is checked for quality indicators and logical inconsistencies. Any implausible findings are returned to the national registries for correction.

Data on year of diagnosis, age and stage at diagnosis were extracted for all GCC nationals newly diagnosed with cervical cancer from 1 January 1998 to 31 December 2012 (N=2,354). Cervical cancer is defined based on the International Classification of Diseases for Oncology, third edition (ICD–O–3) and includes topography codes C53.0 (endocervix), C53.1 (exocervix), C53.8 (overlapping lesion of cervix uteri) or C53.9 (cervix uteri).

Stage at diagnosis is presented as SEER–Summary Stage (Surveillance, Epidemiology, and End Results), which categorizes the extent of disease as: in situ (non–invasive carcinoma in situ or cervical intraepithelial neoplasia grade III), localized, regional (by direct extension only, lymph node involvement only, or both) and distant sites/lymph node involvement. Because in situ data is not consistently collected and not provided by all registries, and because they entail different interpretation in comparison to invasive tumors, these were excluded (n=22).

Time–trends were produced for three 5–year consecutive periods (1998–2002, 2003–2007, and 2008–2012) in order to account for year–to–year fluctuations due to small numbers. Trends in age–specific frequencies and age–specific incidence rates (IRs) by 5–year age groups are presented for the GCC as a whole. IRs for each member state and age group were calculated per 100,000 population using the country’s mid–year female population estimates (nationals only). GCC age–specific IRs are the average of the age–specific IRs of each state.

Trends in numbers of women diagnosed with cervical cancer during 1998–2012, and in age–standardized incidence rates (ASRs) per 100,000 population were produced for each state and as a GCC average. The ASR in each country were estimated by applying the age–specific incidence rates to the world standard population for developing countries using the direct method. This enables comparison of incidence between populations of different age structures and over time. ASR for each
period was obtained by averaging the annual ASRs over the relevant 5-year period. The GCC ASR is an average of the six states’ ASRs in order to avoid the estimate being heavily influenced by the ASR of Saudi Arabia, which makes up 79% of the population of GCC nationals. The distribution of stage at diagnosis for each member state and the GCC as a whole, and trends in stage distribution are shown. ASRs were calculated in the Statistical Analysis System (SAS Version 9.3) and all other analyses were carried out using Stata IC 15 version 3.

Results

A total of 2,332 new cases of invasive cervical cancer were diagnosed among GCC nationals during 1998–2012. The mean age at diagnosis was 40.3 years (Standard deviation=13.8), and the median age was 39.0 years, ranging from 39.7 in the UAE to 43.9 in Bahrain.

The number of women diagnosed with cervical cancer peaked in the age group 35–39 for the two periods 2003–2007 and 2008–2012. A bimodal distribution was observed for the earlier period 1998–2002, with a first peak in the 30–34 age-group and a second one in the 45–50 age-group (Figure 1). The pattern of age distribution also shows a typical steep increase in incidence, followed by a slower decline.

The age–specific incidence rate reached a peak in the 55–59 age–group during 1998–2002 and in the 70–75 age–group during 2003–2007 and 2008–2017, with a slight shift towards older age over the three periods (Figure 2).

The number of cases in the GCC has slowly increased from 712 in 1998–2002 to 846 in 2008–2012, while the ASR has decreased overall and to different degrees for individual GCC states except the UAE (Table 1).

The majority of women (39%) were diagnosed at regional stage. The proportion of unknown stage ranged from 10% in the UAE to 58% in Oman (Figure 3). The proportion of unknown stage has increased over time in Kuwait, Oman, and the UAE, while it remained fairly stable in Qatar and Saudi Arabia. In Bahrain however, the proportion of unknown stage has decreased drastically between 2003–2007 (84%) and 2008–2012 (10%) (Figure 4).

Discussion

We analyze trends in cervical cancer incidence in the GCC States and present them by age and stage. This is an important component in describing the burden of cervical cancer, which is the first step towards setting cancer control strategies.

Cervical cancer occurs in a relatively young age compared to other adult cancers, when many women are still raising families and/or are contributing to the economy. In the young population of the GCC, half of the cases were diagnosed before the age of 40 and 90% before the age of 60, compared to a median age at diagnosis of 47 in the USA. [17]

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Table 1: Number of cases and 5-year average age standardized incidence rates (ASR/100,000 women) for the 3 periods of diagnosis.
Cervical cancer age-specific curves tend to follow curves in HPV prevalence by 20–25 years and have the same shape. This could give an indication of patterns of HPV infection for which population-based prevalence studies are lacking in the GCC. It could also have implications for age of HPV vaccination, should this vaccine be added to the national vaccination schedules. The prevalence of pre-malignant cervical lesions peaks around 10 years preceding the peak of cervical cancer incidence. This can be helpful to set the optimal age for the minimal screening recommended by the WHO. The age-specific incidence patterns have shifted over the study periods from a bimodal curve, which is seen in some

![Figure 3: Distribution of stage at diagnosis by country (SEER Summary Stage), 1998–2012.](image)

![Figure 4: Time-trends in stage distribution (SEER Summary Stage) for each GCC member state by period of diagnosis (%).](image)
populations, to a single peak. The reason for the bimodal curve is unknown but probably follows the bimodal age distribution of HPV prevalence. This may be caused by changes in sexual patterns (a new partner of the woman or her male partner), reactivation of latent HPV infection due to changes in cell-mediated immunity or a cohort effect, which reflects a change in peak age of incidence in the different cohorts of women for which incidence is captured during a given period.\(^{[20]}\)

The age at peak incidence and the age-specific incidence rates seem to be shifting towards older age, this probably reflects both the aging of the population and the delay of marriage, being a proxy for risk of exposure to HPV.

Our 5-year average ASRs for Bahrain, Oman and the UAE during 1998–2002 were similar to those previously reported for the period 1998–2001,\(^{[21]}\) but slightly higher than the ASR published earlier for Bahrain covering the same period (6.4/100,000 versus 4.0/100,000).\(^{[22]}\) This may be due to late registration of cases diagnosed in earlier years leading to increased completeness of our data. The ASRs declined over time for all GCC member states except for the UAE, where it increased during 2008–2012 compared to 1998–2002. The total number of women diagnosed with cervical cancer in the GCC has increased over the 15-year period, but this increase was mainly driven by the increase in Saudi Arabia, which has the largest population in the GCC. Saudi Arabia had a very high fertility rate in the previous century and the large number of women entering the age group at risk may be offsetting the reduction in ASRs, leading to an increase in the absolute counts. The number of women in the GCC states occupying the age group at risk for cervical cancer (older than 20 years) has almost doubled between 1998 and 2012 (Figure 5). The decline in ASR probably reflects some success of the opportunistic screening being offered to varying degrees, and may indicate a change in risk factors, like delay in the age of marriage and childbearing, reduced fertility rates and reduced polygamy. In the 2016 Saudi Arabia demographic survey, over 30% of ever-married women aged 45 and more reported that their first marriage was before age 19, while only 17% of ever-married women aged 25–35 were married by age 19. Previous marriages of the husband may also play a role in risk of exposure to HPV. Of the ever-married surveyed population, only 3% of women versus 13% of men were married more than once.\(^{[23]}\) Smoking, also a risk factor for cervical cancer, is quite low among women in the GCC but may be on the rise.\(^{[21]}\)

While the proportion of women presenting in localized stage varied widely between GCC states, a meaningful comparison cannot be made due to the large variation in unknown stage at diagnosis in Bahrain, Kuwait, Oman and Qatar. Over the 15-years we looked at, the proportion of missing stage has increased with time in Kuwait, Oman and the UAE. This may indicate that an increasing number of women are travelling abroad for staging and treatment after the initial tissue diagnosis. Stage is the most important predictor for cervical cancer survival and monitoring stage at diagnosis gives an indication of the success of cancer control policies. Therefore, efforts should be made to improve the completeness of stage data, including for those who travel abroad. If stage was assumed to be missing at random, the stage distribution of the total GCC population is unfavorable in comparison to the United states for example, where 45% of women present in localized stage.\(^{[24]}\) A review of cervical cancer screening in Arab countries found uptake to be low. For GCC States included in the review (Kuwait, Saudi Arabia, UAE and Qatar), between 16.8% of women surveyed in Saudi Arabia and 37% in Kuwait had a pap–smear at least once in their life. Knowledge of cervical cancer risk factors and availability of screening tests was generally low. Among women who were aware of the test, cultural barriers and fear of pain, in addition to not being offered the test by their physicians, were the main reasons given for not undergoing a pap–test.\(^{[25]}\) In a nationally representative survey conducted in Kuwait, Oman, Saudi Arabia and the UAE in 2008/2009, the proportion of eligible

![Figure 5: Population pyramid of GCC Nationals](image-url)
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women who received a pap—smear within recommended intervals for their age ranged from 7.6% in Saudi Arabia to 28.0% in the UAE.[26] Monitoring the proportion of in situ lesions can also help assess the success of screening efforts. Therefore, these should be routinely registered and reported.

Because not all registries provide data on non—citizens, we could not include this group. Many non—citizens in the GCC are on short—term contracts and return to their home courtiers if they become seriously ill. Nevertheless, this group makes up almost half the population of the GCC and must be accounted for in health—care planning.

Conclusion

There has been a modest decline in ASR for cervical cancer in the GCC in general and a shift towards later age at diagnosis. The majority of women are diagnosed at localized stage. Monitoring trends in the number of individuals diagnosed with cancer over time helps to plan future diagnostic and treatment services, while trends in age—specific incidence patterns give an indication of changing risk factors. Age—standardized incidence rates also could reflect changes in risk factors and highlight the extent of effectiveness of preventive measures. The distribution of stage at diagnosis reflects the success of both screening and early diagnosis. Efforts to collect more complete stage data should be made as stage at diagnosis is the most important determinant of survival for cervical cancer.

References


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