Global Disparities in Cervical Cancer: Literature Review

Data Analytics and Visualization Project

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Introduction

Cervical cancer is the fourth most common cancer affecting women, and according to the latest statistics from the International Agency for Research on Cancer (2021), there were 604,237 new cases and 341,831 deaths due to cervical cancer in 2020. In most parts of the world, the age-standardized rates[1] of incidence and deaths from cervical cancer have been slowly decreasing over the past few decades, largely due to the introduction of school programmes for HPV vaccinations and national screening programmes (Sung et al., 2021). However, in many countries (such as Lesotho, Zimbabwe, and Bulgaria) the incidence and mortality rates are actually increasing, and women in low-resource settings are still disproportionately affected by cervical cancer (Zhang et al., 2021).

What is Cervical Cancer?

Cervical cancer (CC) is a cancer that develops in a person's cervix (the entrance to the uterus from the vagina).[2] Despite CC being so common, it is an extremely preventable type of cancer as it progresses very slowly (WHO, 2006). 99% of cervical cancers are caused by one or more of the high-risk oncogenic types of human papillomavirus (HPV). HPV is a common sexually transmitted infection, and most cases resolve themselves 1-2 years after exposure, but the small proportion of infections that persist for many years are strongly linked to a high risk of diagnosis of precancer (Schiffman et al., 2007). Thus, immunization against HPV has been proven to be highly effective at preventing the development of CC (Lei et al., 2020). Screening for and treating precancerous lesions is also an extremely effective secondary prevention approach, and the earlier that the cancer is diagnosed, the easier it is to treat and the higher the survival rate.

Disparity in CC Rates

There are huge disparities in the rates of CC around the world. In 23 countries, it is the most commonly diagnosed cancer for women, and in 36 countries, it is the leading cause of cancer deaths for women

[1] All rates mentioned in this review are age standardized.

[2] Please note that while this project will refer to data about women, cervical cancer can affect any person who has a cervix. Unfortunately, there is not global cervical cancer data available for trans-men, non-binary or other gender expressions, and it is unclear if they have been included in the statistics for women.

(Sung et al., 2021). Most of these countries are in Sub-Saharan Africa, Melanesia, South America, and South-Eastern Asia. The highest regional rates of CC are in Africa, especially eastern, southern, and western Africa where the rates are 7 to 10 times higher than in regions like North America, Australia/New Zealand, and Western Asia (Iraq and Saudi Arabia) (Bray et al., 2018).

Inequalities in CC rates are not just between regions and countries; research shows that there can also be disparities within developed countries due to factors such as income or education level (Jolidon et al., 2020). For example, in the United States, a study showed that the CC mortality rates were doubled in areas of high-poverty compared to low-poverty areas (Siegel et al., 2019).

While CC is a very preventable disease, low-income and middle-income countries (LMICs) tend to have poorer access to preventative services compared to richer countries, as well as less access to treatment for the later stages of the disease (Anaman-Torgbor et al., 2020). As a result, there are significantly higher mortality rates in these countries, and of the 310,000 women who died of this disease in 2018, 90% were living in LMICs (Fray et al., 2020). Not only is CC the leading cause of cancer deaths for women in many developing countries, but the average age at death is younger compared to other cancers, meaning there are more years of life lost, and these younger women are more likely to have been still raising families (Yang et al., 2004).

Anaman-Torgbor and colleagues (2020) studied screening challenges in Sub-Saharan Africa and found that most countries did not have national screening programmes due to competing funding priorities, low prioritization of CC, and not having enough trained staff. They also identified barriers such as rural women having limited access to screening centres as they were mostly located in urban areas. Even when women could access screening services, there was still a low uptake of these services due to socio-cultural barriers, such as lack of knowledge about the seriousness of the disease or preference for traditional healers over western medicine.

Risk Factors

In addition to persistent HPV infections, there are other co-factors that increase a person's risk of developing CC - including sexually transmitted diseases like HIV and Chlamydia trachomatis, smoking, and the use of oral contraception (Murillo et al., 2016).

Research shows that high parity (number of previous pregnancies of >20 weeks) is another risk factor, and Tekalegn et al. (2021) estimated that women who have given birth to three or more children have 2.4

times higher odds of developing CC compared to women with parity of less than three. Furthermore, Drain et al. (2002) analysed data from 127 LMICs, and their results showed that high rates of the disease were not only significantly associated with increased fertility, but they were also linked to high rates of teenage pregnancy and early age at birth of first child. Thus, females living in societies where there are high birth rates and high rates of teenage pregnancy, such as Sub-Saharan Africa, are even more at risk of developing CC, and Neal et al. (2020) have found that it is the poorest women living in rural areas in these countries who are most likely to give birth while they are still adolescents.

HIV also significantly increases a woman's risk of developing CC, and a study by Stelzle et al. (2021) estimates that in southern Africa 63.8% of women with CC are living with HIV, while 27.4% of women with CC have HIV in eastern Africa. And their analysis showed that there were more than 20 women per 100,000 in these regions with CC that is attributable to HIV, meaning that countries with high rates of HIV have the added burden of HIV-attributed CC to the already substantial CC burden.

CC and Human Development

The Human Development Index (HDI) was created by the United Nations Development Programme as a summary measure of average achievement in key dimensions of human development (health, education, and standard of living). Mansori et al. (2018) used linear regression models to assess the associations with CC rates and the different components of HDI. They discovered that regions with low and medium HDI tend to have higher rates of both incidence and mortality, and that each of the components of HDI has a significant negative association with rates of CC. These components include life expectancy ($B=-0.98$, $P<0.001$), mean years of schooling ($B=-1.86$, $P<0.001$), and gross national income ($B=-0.38$, $P<0.001$).

Another study used Ordinary Least Squares and Poisson regression models to assess the effect HDI, Gender Inequality Index (GII) and other socioeconomic factors (like poverty, health expenditure per capita and literacy) have on CC rates (Singh et al., 2012). They found that not only were all these variables significantly correlated with incidence and mortality rates, but HDI and poverty rate each explained >52% of the global variance in mortality. Furthermore, their results suggested that there would be a 20% decrease in CC risk and a 33% decrease in CC mortality risk for a 0.2 unit increase in HDI.

Reducing the Global Burden

In November 2020, the World Health Organization launched a global strategy to eliminate cervical cancer with the aim of reducing the number of cases to a threshold of 4 per 100,000 women. They are calling on countries to meet the following targets by 2030: 90% of girls fully vaccinated with the HPV vaccine by

age 15 years, 70% of women are screened with a high-performance test by 35 years of age and again by 45, and 90% of women identified with cervical cancer receive treatment (WHO, 2020).

While it is still too early to evaluate the impact of the WHO initiative, action is already being taken around the world to introduce more national HPV vaccine programmes. Bruni et al. (2016) found that between 2006 and 2014, only 64 countries nationally, 4 countries subnationally, and 12 overseas territories had implemented HPV vaccination programmes. And in 2018, only 4 LMICs reported good coverage levels for the HPV vaccine, and these initiatives were all funded by external funders (Spayne & Hesketh, 2021). Whereas, according to the latest data from PATH, 117 WHO member states and 27 non-members now have active HPV vaccination programmes, with a further 33 expected to introduce programmes by 2023. However, despite this progress, only 35% of LMICs have implemented national HPV immunization programmes thus far, compared with 88% of high-income countries (PATH, 2021).

Brisson et al. (2020) estimate that meeting both the vaccination and screening WHO targets would avert more than 74 million cervical cancer cases in LMICs over the next century, or 61 million cases for just meeting the vaccination target. Their study also showed that screening is crucial for elimination in countries with the highest incidence rates.

As the link between HPV and CC is now clear, HPV DNA testing is a new form of screening that WHO recommends for countries with limited resources as a more affordable alternative to the conventional Pap cytology-based test (Vu et al., 2018). However, it is still highly dependent on laboratories, and so may not be suitable for all settings. Other alternatives to consider are direct visual inspection with acetic acid (combined with cryotherapy for early cervical lesions) and self-sampling at home; these are more feasible and accessible options for increasing screenings in developing countries, but they have other disadvantages such as lower specificity (Arbyn et al., 2018).

Innovative technologies also have the potential to support cost-effective prevention methods. For example, William et al. (2018) compared different applications of image analysis and machine learning techniques that aim to automate the diagnosis and classification of CC from Pap smear images. These types of classifiers have the potential to greatly aid visual inspection screenings. Other studies have focused on using algorithms to calculate a person's risk of developing CC based on their answers to a survey about different risk factors (Unlersen, Sabanci & Özcan, 2017). Such models could help with prioritizing the most at-risk women for screening in low-resource settings.

Conclusion

Research shows that the poorest women in the world are the most affected by CC, and despite CC being a very preventable disease, it continues to be a major public health burden, especially in LMICs. While low resources and poor health infrastructure are two of the most common factors attributed to the stark differences in global CC rates, there are other socio-cultural factors that also need to be considered. And research indicates that there is a strong link between CC rates and disparities in human development, gender inequality, and access to education and resources. While WHO is aiming to eliminate CC in the next century, the affordability of prevention strategies remains a major barrier to achieving this goal, and technology such as machine learning techniques could play a role in making cost-effective methods more efficient. Finally, it is crucial that women everywhere receive sufficient sex education and are made aware of the risks of CC, and that they are empowered to make choices and seek services that protect their sexual and reproductive health.

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