Hospitalization Rates of Human Papillomavirus-Associated Cancers in Brazil from 2011 to 2019

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Introduction

- Human papillomavirus (HPV) infection can cause several diseases, such as genital warts, recurrent respiratory papillomatosis, and cancers including some anogenital and head and neck cancers¹
- Brazil has limited population coverage data availability from cancer registries.²
 However, the inpatient database (Sistema de Informações Hospitalares do Sistema Único de Saúde [SIH-SUS]), which covers 75%-80% of the Brazilian population, offers a valuable opportunity to access information on the burden of HPV-associated cancers
- In Brazil, HPV vaccination program started in 2014 for girls (11-14 years) and in 2017 for boys (11-14 years). The program has progressively expanded to include individuals aged 9-45 years living with human immunodeficiency virus (HIV)/

Figure 1. Percentage of HPV-associated cancers

A. HPV-associated cancers in both genders. **B.** HPV-associated cancers in females. **C.** HPV-associated cancers in males.



acquired immunodeficiency syndrome (AIDS), cancer, transplant recipients, recurrent respiratory papillomatosis, victims of sexual violence, and those using pre-exposure prophylaxis^{3,4}

Objective

To describe the burden of HPV-associated cancers in Brazil from 2011 to 2019.

Methods

- This was a descriptive analysis on HPV-associated cancer hospitalizations, using secondary data from the inpatient database of the Brazilian public healthcare system (SIH-SUS)
- HPV-associated cancers were defined as cancers occurring at anatomic sites where HPV DNA is frequently detected; HPV-attributable cancer was defined as a cancer probably caused by HPV. The attributable fraction was estimated using polymerase chain reaction (PCR) studies for HPV DNA detection, except for head and neck cancers, which also considered p16 positivity⁵⁻⁶
- Hospitalizations were identified using International Classification of Diseases (ICD-10) codes. Average annual hospitalization rates were expressed per 100,000 population
- The hospitalization rate trends for each HPV-associated cancer were analyzed using joinpoint analysis. Trends were assessed using the average annual percent change (AAPC); a trend was considered to be increasing or decreasing if *p*<0.05; otherwise, the trend was stable

Table 1. Average annual numbers and hospitalization rates of HPV associated and attributable cancers by anatomic site in Brazil, 2011-2019

	HPV-associated cancers			HPV-attributable cancers
Anatomic site	Average no. of hospitalizations (rate ^a) 2011-2019	Trends AAPC 2011-2019	Attributable fraction	Average no. of hospitalizations (rate ^a) 2011-2019
Cervix	21,670 (20.9)	-0.4 (-1.4; 0.4)	100%	21,670 (20.9)
Vagina	472 (0.5)	4.3* (1.1; 8)	78.0%	368 (0.4)
Vulva	714 (0.7)	1.2 (-0.1; 2.5)	48.0% (<60 years) 15.0% (≥60 years)	195 (0.2)
Penis	1,922 (1.9)	2.3* (1; 3.7)	51.0%	980 (1.0)
Anus, males	1,126 (1.1)	4.8* (3.5; 6.2)	100%	1,126 (1.1)
Anus, females	1,902 (1.8)	4.8* (2.8; 6.3)	100%	1,902 (1.8)
Larynx, males	9,887 (9.9)	3.1* (1.7; 4.6)	4.5%	445 (0.4)
Larynx, females	1,697 (1.6)	1.6* (0.4; 2.9)	4.5%	76 (0.1)
Oropharynx, males	5,661 (5.7)	2.4* (1.4; 3.5)	22.1%	1,251 (1.3)
Oropharynx, females	1,310 (1.3)	1.4* (0.3; 2.6)	22.1%	290 (0.3)
Oral cavity, males	5,528 (5.6)	-0.5 (-1.9; 0.9)	6.3%	348 (0.3)
Oral cavity, females	2,224 (2.1)	-0.9 (-3.9; 2.6)	6.3%	140 (0.1)
All HPV cancers, females	29,989 (28.9)	0.1 (-0.3; 0.6)		24,642 (23.7)
All HPV cancers, males	24,124 (24.2)	2.2* (1.3; 3)		4,151 (4.2)
All HPV cancers, both sex	54,113 (26.6)	1.0*(0.3; 1.5)		28,793 (14.2)

Results

HPV-associated cancers

- From 2011 to 2019, a total of 487,017 hospitalizations due to HPV-associated cancers were reported, with 269,901 (55%) in females and 217,716 (45%) in males. On average, there were 54,113 annual hospitalizations (26.6/100,000), including 29,989 for females (28.9/100,000) and 24,124 for males (24.2/100,000) (Table 1). The Figure 1A presents the distribution of HPV-associated cancer in both genders
- Cervical cancer was the primary cause of hospitalizations among females, accounting for 72% of hospitalizations (Figure 1B). Selected head and neck cancer sites (oral cavity, oropharynx, and larynx) were the predominant reason for hospitalizations among males (87.4%) (Figure 1C)
- For females, there has been a significant increasing trend in hospitalization rates for vaginal, anal, laryngeal, and oropharyngeal cancers at an annual rate of 4.3%, 4.8%, 1.6%, and 1.4% for 2011-2019. For males, increasing trends in hospitalization rates were seen in penile cancer (4.3% per year) and, similarly to females, in anal, laryngeal, and oropharyngeal cancers, at an annual rate of 4.8%, 3.1%, and 2.4%, respectively (Table 1)

Estimates of attributable fraction of HPV-associated cancers

An estimated 259,133 HPV-attributable hospitalizations occurred, with an average of 28,793 hospitalizations per year, including 24,642 among females and 4,151 among males (Table 1). The most common causes of HPV-attributable cancers were cervical and selected head and neck cancers for females and males, respectively. For both genders, selected head and neck cancers represented 8.9% (2,550 hospitalizations

^aExpressed as per 100,000 population.

Limitations

 Attributable fraction estimates: Using attributable fraction estimates derived from PCR studies for HPV DNA detection may be not sufficient for causal association and led to inaccuracies in estimating the burden of HPV-attributable cancers



References

- 1. Meites E, et al. https://www.cdc.gov/pinkbook/hcp/table-of-contents/chapter-11-human-papillomavirus.html. Accessed September 15, 2024.
- 2. E Silva DRM, et al. BMC Cancer. 2024;24(1):870.
- 3. Ministerio da Saúde Brasil. https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/notas-tecnicas/2024/ nota-tecnica-no-41-2024-cgici-dpni-svsa-ms. Accessed September 15, 2024.
- 4. Ministerio da Saúde Brasil. https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/notas-tecnicas/2024/ nota-tecnica-conjunta-no-101-2024-cgici-dpni-svsa-ms/. Accessed September 15, 2024.
- 5. de Martel C, et al. Lancet Glob Health. 2020;8(2):e180-e190.
- 6. Sichero L, et al. *Head Neck.* 2022;44(1):122-133.

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- Database limitations: The SIH-SUS database does not allow for the analysis of individual patients, and the same patient may be hospitalized multiple times
- Underestimation of total burden: Patients treated in private system (~20%-25%) were not accounted for

Conclusion

 There is a substantial burden of HPV-associated cancers in Brazil, with increasing trends in hospitalization rates observed in some HPV-associated cancers, affecting both males and females. To reverse this trend, it is essential to expand HPV vaccination for older cohorts, increase early-stage cancer diagnosis efforts, and improve treatment and supportive care for individuals with advanced or metastatic HPV-associated cancers to improve outcomes nationwide