Kongrtay *et al. J Cancer Metastasis Treat* 2023;9:32
DOI: 10.20517/2394-4722.2023.54

Journal of Cancer Metastasis and Treatment

Original Article

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Prevalence of high-grade HPV types among women in Astana, Kazakhstan (2018-2022)

Kuralay Kongrtay[1], Nazira Kadrlodinova[1], Fatima Sultankulova[2], Aigul Batpanova[2], Yevgeniy Kim[2], Danagul Zhumasheva[3], Nasrulla Shanazarov[4], Nazira Kamzayeva[2]

[1]Department of Surgery, School of Medicine, Nazarbayev University, Astana 010000, Kazakhstan.
[2]Clinical Academic Department of Women's Health, University Medical Center, Astana 010000, Kazakhstan.
[3]Medical Outpatient Clinic, Limited Liability Company "Densaulik Astana", Astana 010000, Kazakhstan.
[4] Center for Photodynamic Therapy, Medical Centre Hospital of President's Affairs Administration of the Republic of Kazakhstan, Astana 010000, Kazakhstan.

Correspondence to: Dr. Nazira Kamzayeva, Clinical Academic Department of Women's Health, University Medical Center, Turan Ave. 32, Astana 010000, Kazakhstan. E-mail: nazira.kamzaeva@umc.org.kz

How to cite this article: Kongrtay K, Kadrlodinova N, Sultankulova F, Batpanova A, Kim Y, Zhumasheva D, Shanazarov N, Kamzayeva N. Prevalence of high-grade HPV types among women in Astana, Kazakhstan (2018-2022). *J Cancer Metastasis Treat* 2023;9:32. https://dx.doi.org/10.20517/2394-4722.2023.54

Received: 1 Jun 2023 **First Decision:** 24 Jul 2023 **Revised:** 30 Jul 2023 **Accepted:** 21 Aug 2023 **Published:** 6 Sep 2023

Academic Editors: Ciro Isidoro, Gunnar Kristensen **Copy Editor:** Fangyuan Liu **Production Editor:** Fangyuan Liu

Abstract

Background: Cervical cancer is a significant public health concern worldwide, and human papillomavirus (HPV) is the leading cause of this disease. While there have been some studies on the prevalence of HPV in Kazakhstan, the country faces unique challenges in preventing and treating HPV-related diseases, including limited resources, a lack of awareness about HPV, and cultural attitudes toward sexual health. This research article aims to provide a comprehensive overview of HPV genotype distribution in Astana, Kazakhstan, for the last five years.

Methods: A cross-sectional study was performed from 2018 to 2022. Study population: Kazakhstani women referring to "Olympus laboratories network" settings for HPV testing age 18-64. AmpliSens® Real-Time PCR kits for HPV genotyping 14 high-risk HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68) were performed.

Results: This study revealed the increasing trend in HR-HPV prevalence among women for five sequential year periods. As a result, approximately 43% of women referred to the HPV testing were HR-HPV positive, with the most prevalent type being HPV 16 (20%), followed by HPV types 31, 52, 51.

Conclusion: By examining the latest research on HPV and cervical cancer in Kazakhstan, we hope to contribute to

developing effective public health policies and interventions to help reduce these diseases' burden in this country. Furthermore, the database will be established for future large-scale studies after vaccination implementation.

Keywords: Human papillomavirus, prevalence, genotype, cervical cancer

INTRODUCTION

The estimated global incidence rate of cervical cancer is 13.3 cases per 100,000 women[1,2]. The burden of cervical cancer remains high in many parts of the world, depending on substantial geographical and socio-economic factors[3,4]. The incidence of cervical cancer remains high among Kazakhstani women of all ages, with an estimated incidence rate of 18.2 per 100,000 women[5-7]. Cervical cancer ranks as the second leading cause of female cancer and cancer-related death among Kazakhstani women, with an estimated 1,777 new cervical cancer cases diagnosed and 834 deaths annually[5,8,9]. Approximately 80%-95% of cervical cancer cases have been linked to human papillomavirus (HPV) infection[8,10,11]. HPV is a small non-enveloped, double-stranded DNA virus of the Papillomaviridae family that is a causative agent for different benign and malignant diseases[12,13]. More than 200 HPV types are known to have a strong association with anogenital cancers, out of which 15 types are identified as high-risk HPV (HR-HPV): HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82[13,14]. HR-HPV types 16 and 18 are responsible for approximately 70% of all cervical cancer cases worldwide, while the other high-risk types (31, 33, 35, 45, 52 and 58) are responsible for 20% of cervical cancer cases[8,10,15]. While over 50% of sexually active females may test positive for HPV, the majority of HPV infections will naturally clear up without leading to any significant outcomes; however, a minority of them will experience the onset of cervical cancer. Factors that increase the risk of both HPV infection and cervical cancer encompass the age at which sexual activity begins, engaging in sexual relationships with multiple partners, smoking, infection with herpes simplex virus, presence of HIV, and co-infection with other genital infections[9,16].

The prevalence of HPV infection and genotype distribution differ across nations worldwide. Earlier reports show higher HPV prevalence in developing countries (42.2%) in comparison with developed countries (22.6%)[17]. According to recent research regarding the geographic HPV genotype distribution, HPV31 and HPV 33 are more prevalent in European countries, whereas in Asian and African regions, HPV 52 and HPV 58, HPV 35, and HPV 45 are more frequent, respectively[18,19]. In addition, several studies were conducted to reveal the HPV epidemiology in different regions of Kazakhstan[20-23]. Nonetheless, the available data on the actual magnitude of HPV infection in Kazakhstan is still insufficient. This manuscript aims to analyze HPV-type diversity among Astana women. Therefore, new data acquisition will establish the database on the prevalence and distribution of HPV genotypes among different areas before HPV-vaccine implementation by providing crucial information for decisions on the HPV vaccination and cervical cancer screening programs.

METHODS

For this retrospective cross-sectional study, a total of 43,061 female patients enrolled who attended Olympus Laboratory in Astana between 2018 and 2022. This study was approved by the Ethics Committee of the joint venture "Olympus Laboratories network" of LLP "Myrza-khan" accredited by the International Organization for Standardization (ISO 15189). The qualitative HPV DNA testing was performed from a cervical smear taken using the cytological brush. The laboratory network used an AmpliSens® Real-Time PCR kit for HPV genotyping (InterLabService, Moscow, Russia) that identifies 14 high-risk HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68) on the CFX 96 Real-Time PCR machine (Bio-Rad Laboratories). DNA extraction and genotyping were performed following the manufacturer's instructions.

Statistical analysis was performed using STATA 16 (StataCorp, 2019). Data analysis included descriptive statistics of mean values, standard deviations, and frequencies, where applicable. Based on the data set obtained from the HPV DNA qualitative testing, the prevalence of HPV genotypes, descriptive statistics, and one-way analysis of variances were calculated.

The Ethics Committee of the joint venture "Olympus laboratories network" approved the study on March 4, 2023 (Number 178). The privacy and confidentiality of the gathered data were ensured.

RESULTS

In total, 43,061 women participated in the study in the period between 2018 and 2022. In 2018, 5,735 women underwent PCR testing for HR-HPV; in 2019, 7,570 women; 8,279 women were recruited in 2020, 11,097 women in 2021, and 10,380 women in 2022 [Table 1]. For five years, out of the total number of participants, 43.68% (n = 18,810) were infected with HR-HPV [Figure 1]. From the results in Table 1, the increasing recruitment of female participants can be observed, as well as the increasing trend in HPV 16 prevalence among these study participants.

Among these positive samples, the most prevalent types detected were HPV 16 (20.1%), HPV 31 (9.04%), HPV 52 (8.5%), HPV 51 (8.1%), and HPV 39 (7.6%) for a 5-year period [Figure 2].

Moreover, several studies have demonstrated that the prevalence and distribution of HPV in Kazakhstan are influenced by geographical variations[15,20,21,24,25]. In this study, we have expanded upon these findings by gathering region-specific data from Kazakhstan and conducting a comparative analysis of HPV prevalence across different regions in Kazakhstan from 2013-2022 [Table 2]. As a result, Table 2 includes the most prevalent five HR-HPV types reported in the previous studies. We found six studies that covered eight cities in Kazakhstan but with various sample sizes and analysis types. All the studies included a general population with both normal and abnormal cytology/histology findings. Our review of previously published articles revealed that HPV16 type was more prevalent in Western regions of Kazakhstan (8%-26%), whereas HPV-45, HPV-59, HPV-35, and HPV-66 were prevailing in southern and eastern regions of Kazakhstan. HPV-31 was found to be the second most common HPV type in the regions such as Astana, Almaty, and the Western area (Aktobe, Atyrau, and Uralsk) in all studies. HPV-18 was included in the five most common types only in Almaty, Aktobe, and Astana, according to the studies conducted between the period of 2013 and 2021.

DISCUSSION

The occurrence and distribution of HPV infections vary worldwide, and the effectiveness of vaccines in providing immunity differs as well[26,27]. Among women with normal cytology results, HPV16 is frequently reported in North America and Europe, while HPV 52 is more common in Asia, including Japan and Taiwan regions[28]. Previous studies conducted across various parts of Asia have shown that the prevalence of HPV among women with normal cytology ranged from 14.0% in southeastern Asia to 14.4% in south-central Asia[29,30]. In these studies, HPV was found in almost 90% of the population with cervical cancer, with the lowest prevalence in mainland China/Hong Kong/Taiwan (82.5%) and the highest in the southeastern area (91.1%)[29,31]. Comparatively, the prevalence of HPV in the Korean population was higher than the prevalence of HPV in the prior analysis in Kazakhstan[31]. Multiple infections were found in 38.1% of HPV-positive cases, with an overall prevalence of HR-HPV at 22.2%[32-34]. However, studies in other Asian countries also demonstrate the unequal prevalence of HPV among different regions within a single country[35,36]. These variations in HPV prevalence can be attributed to various factors such as virus- and vaccine-related, socio-economic, geographical as well as cultural factors[37-39].

Table 1. Distribution of HPV types in 2018-2022

HPV type	2018 (total *N* = 5,735) % of positive	2019 (total *N* = 7,570) % of positive	2020 (total *N* = 8,279) % of positive	2021 (total *N* = 11,097) % of positive	2022 (total *N* = 10,380) % of positive
16	20.90	18.23	19.84	21.74	19.91
18	5.29	5.14	4.87	4.04	4.26
31	9.29	9.46	9.48	8.26	8.73
33	4.37	4.32	3.96	3.98	4.12
35	4.40	4.66	3.87	4.26	5.12
39	8.36	6.94	7.54	7.72	7.29
45	4.40	4.69	3.93	3.80	4.53
51	7.40	8.92	8.39	7.46	8.15
52	8.32	8.58	7.98	9.10	8.57
56	6.10	7.43	7.25	7.18	7.12
58	4.92	5.60	5.55	5.01	4.95
59	4.81	3.96	4.46	4.56	4.62
66	4.96	5.72	5.31	5.36	5.08
68	6.47	6.36	7.57	7.54	7.54

This current research represents the first large-scale study conducted in the Central Asian countries, analyzing data for the past 5-year period. The study revealed that nearly half of the participants who were referred for HPV testing had positive results. Although the reported prevalence of HPV types varied in prior studies conducted in Kazakhstan, our findings are consistent with them. Our investigation indicated that HPV16 was the most prevalent among 14 high-risk types, with a prevalence of 20% over the last 5 years [Table 1]. These results align with the previous studies where HPV16 distribution varied from 10,6% to 27.7% in the Western region of Kazakhstan and 18.4% in Astana[20,21]. In a recent study by Babi *et al.* (2021), which covered various regions of the country, HPV16 was found in 54% of single infections and 57% of multiple infections[24]. Although HPV16 remains the most prevalent type in the Kazakhstani population, the prevalence of other HPV genotypes differs between studies. Our study identified HPV-31, HPV-52, HPV-51, HPV-39, and HPV-68 as the next most prevalent types, but with a significant difference in prevalence compared to HPV-16. In previous studies conducted in Kazakhstan, HPV-31, HPV-51, and HPV-52 were also commonly reported after HPV-16, albeit with varying prevalence rates [Table 2]. A study conducted in Western Kazakhstan by Junerbayeva *et al.* (2015) reported the most common types as HPV16 (27.7%), HPV31 (13.6%), HPV52 (9.9%), HPV18 (9.6%), and HPV33 (3.6%)[40]. From Figure 1, it is evident that the prevalence of HR-HPV has been increasing in Kazakhstan (Astana) over the past 5 years. Previous studies have reported the occurrence of HPV infection in Kazakhstan ranging from approximately 44% to 56%, with the most common HPV types being 16 (10.7%-27.7%), 18 (9.2%-9.6%), 51 (5%), and 33 (3.6%-5%) [Table 2][5]. The previous pilot study conducted in Astana reported a total HPV prevalence of 43.6%, which is comparable to our findings despite the significant difference in sample size[21]. In comparison to the central part of Kazakhstan, the western regions showed a 26% HPV infection rate among both females and males[20]. A recent analysis that included cities from all four regions of Kazakhstan found that the prevalence of single HR-HPV infection was 26%, while 13% of the study population had multiple HPV infections[24]. These results highlight the variation in frequently reported HPV types even within the same country[36,37,41]. Various studies have shown the diversity in HPV genotype distribution within Kazakhstan; however, the understanding of HPV-related cancer prevalence in the country remains unclear[13,15,22,24]. Limitations of this study include the lack of analysis regarding socio-demographic aspects, as well as the association with cytology or histological findings. Additionally, age-specific categorization is crucial for defining the risk factors for HPV acquisition. Furthermore, this study serves as a preliminary investigation, laying the foundation for future extensive research.

Table 2. Prevalence of HPV genotypes in Kazakhstan

Country	Region	Sample type study type	Sample size	Age	Collection period	Overall prevalence, %	HPV genotypes, %				
Kazakhstan	Astana	Current study	43,061	18-65	2018-2022	43.68	HPV16 (20%)	HPV31 (9,0%)	HPV52 (8,5%)	HPV51 (8,1%)	HPV39 (7,6%)
Kazakhstan[22]	Astana	Cross-sectional survey-based	759	26-35	May 2019-Dec 2020	39	HPV35 (21%)	HPV31 (18%)	HPV68 (15%)	HPV16 (12%)	HPV45 (10%)
	Almaty						HPV45 (60%)	HPV31 (50%)	HPV18 (46%)	HPV66 (44%)	HPV52 (42%)
	Aktobe						HPV59 (53%)	HPV56 (50%)	HPV18 (24%)	HPV16 (22%)	HPV31 (21%)
	Oskemen						HPV35 (52%)	HPV58 (42%)	HPV51 (41%)	HPV39 (38%)	HPV68 (38%)
	Pavlodar						HPV66 (36%)	HPV51 (28%)	HPV33 (20%)	HPV16 (18%)	HPV52 (18%)
Kazakhstan[14]	Astana	Cross-sectional survey study	1,645	26-35	May 2019-Dec2020	16	HPV39 (16%)	HPV51 (16%)	HPV68 (15%)	HPV52 (11%)	HPV31 (8%)
	Almaty						HPV68 (33%)	HPV52 (26%)	HPV51 (15%)	HPV58 (15%)	HPV59 (15%)
	Aktobe						HPV56 (20%)	HPV31 (16%)	HPV59 (15%)	HPV68 (13%)	HPV68 (13%)
	Oskemen						HPV68 (34%)	HPV58 (16%)	HPV51 (13%)	HPV59 (10%)	HPV33 (8%)
	Pavlodar						HPV31 (41%)	HPV51 (16%)	HPV66 (11%)	HPV52 (10%)	HPV39 (10%)
Kazakhstan[19]	Astana	Pilot study	140	18-59	Dec 2015-Apr 2016	43,6	HPV16 (18%)	HPV18 (9,2%)	HPV33 (4,9%)	HPV51 (4,9%)	HPV52 (4,9%)
Kazakhstan Western[18]	Aktau	Retrospective analysis	1,661	16-66	2013-2014	26	HPV16 (17%)	HPV51 (6.4%)	HPV33 (6.4%)	HPV56 (4.3%)	HPV39 (2.1%)
	Atyrau						HPV16 (17%)	HPV31 (6.4%)	HPV39 (6.4%)	HPV45 (4.5%)	HPV56 (3.6%)
	Uralsk						HPV16 (9.62)	HPV31 (5.8%)	HPV51 (5.7%)	HPV39 (4.8%)	HPV56 (3.8%)
	Aktobe						HPV16 (8.7%)	HPV39 (6.3%)	HPV51 (5.9%)	HPV56 (5.0%)	HPV18 (4.6%)
Western Kazakhstan[23]		Multipurpose research	1,166	18-60+	2014-2017	25	HPV16 (26%)	HPV31 (10%)	HPV51 (9.0%)	HPV52 (9.0%)	HPV 6 (7.9%)

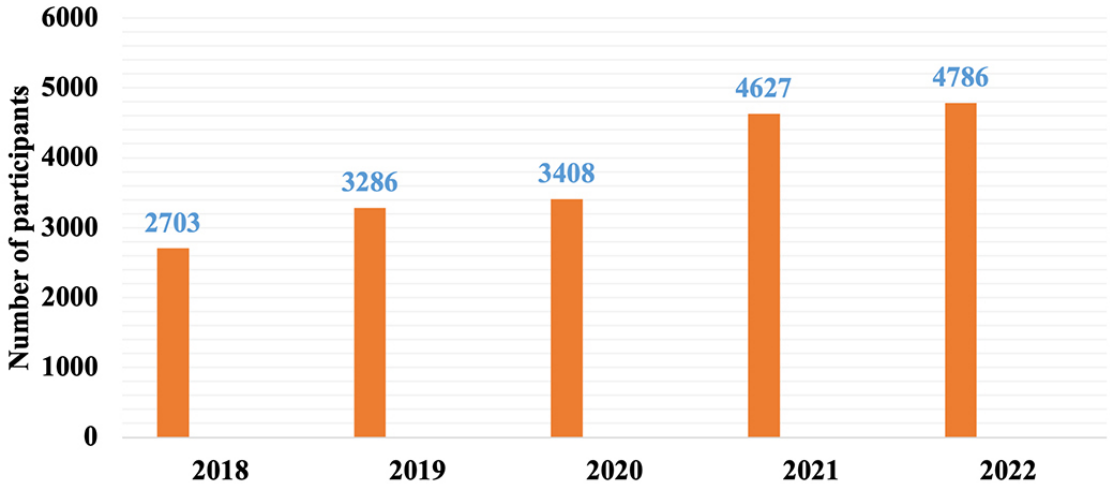

Figure 1. Prevalence of HPV infection in Astana from 2018-2022.

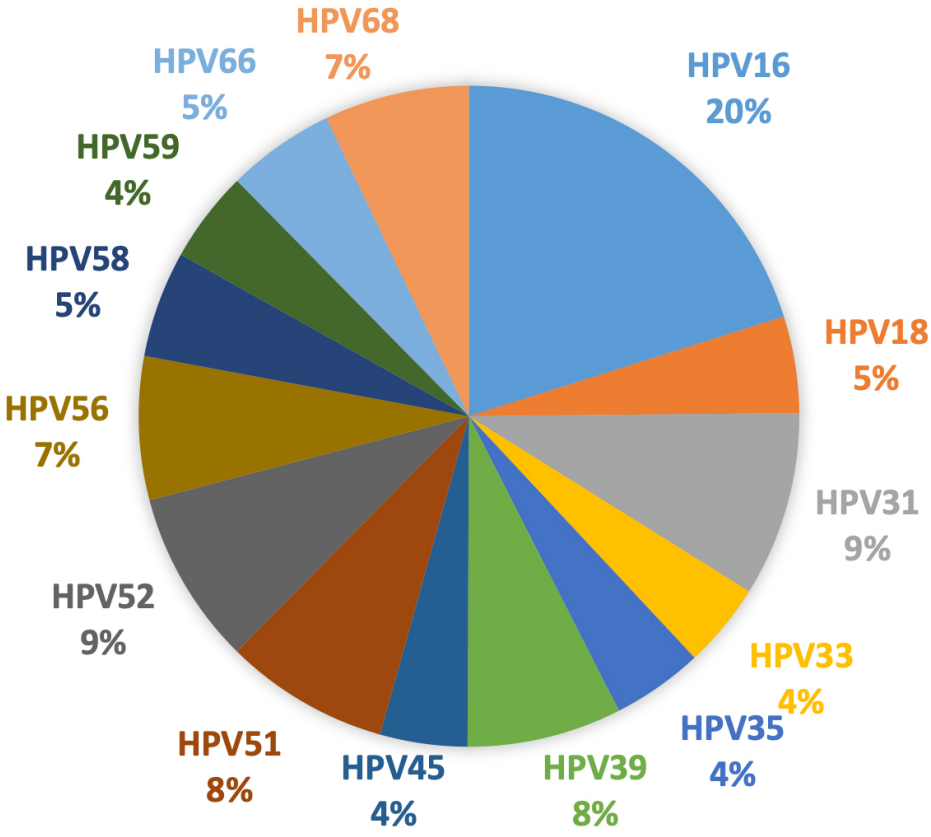

Figure 2. Distribution of HPV types in Kazakhstan for the last five years.

Currently, the cervical cancer prevention program in Kazakhstan does not include screening for HPV infection and is undergoing changes in the administration of HPV vaccination as a primary preventive measure[22,42-44]. Moreover, the cost-effectiveness of HR-HPV testing should be considered in terms of financing and availability, as HPV testing is not covered by the government or insurance, with a limitation

to only HPV-16 and 18[25,45-47]. The results of this study emphasize the need for further research to assess the prevalence of all HR-HPV types among the general population in Kazakhstan, including both males and females, in order to understand the burden of HR-HPV-associated diseases. Additionally, there is a need to expand the national cervical cancer prevention program to include more comprehensive screening methods beyond routine Pap smear tests.

CONCLUSION

Overall, these studies indicate that HPV is relatively common in Kazakhstan. Prevention efforts such as HPV vaccination and regular cervical cancer screening are important for reducing the burden of HPV-related diseases in the country. However, it is essential to note that the prevalence of HPV may have changed since the time of these studies, and further research is required to fully comprehend the current nationwide situation. The findings of our current study provide crucial information as a basis for future comprehensive studies, particularly after the implementation of the vaccination program in Kazakhstan in 2024.

DECLARATIONS

Acknowledgments

We sincerely thank the staff of the Russian-Kazakh joint venture "Olympus laboratories network" for their collection of samples for this study.

Authors' contributions

Designing the study: Kadrlodinova N
Writing the manuscript: Kongrtay K, Kadrlodinova N
Performing the statistical calculations and analysing: Kongrtay K, Kadrlodinova N, Sultankulova F
Revising the manuscript before submission: Shanazarov N, Kamzayeva N
Taking part in the interpretation of the results: Batpanova A, Zhumasheva D
All authors have read and approved the final version of this manuscript.

Availability of data and materials

All data described in the manuscript are available.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

This study was reviewed and approved by the Ethics Committee of the joint venture "Olympus laboratories network" on March 4, 2023 (extract #178). All participants signed a written informed consent form.

Consent for publication

Not applicable.

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