



Genotype Prevalence and Distribution of Human Papillomavirus Among Women in North-West Region of Romania

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Abstract

The purpose of this study is to identify which types of Human Papillomavirus (HPV) are more frequently met in females from North-West of Romania and to establish the distribution of HPVs among women, regarding the age. The cases were collected from Resident Laboratory from Oradea city, Romania in a time interval between 01.01-31.12.2022. The cases were gathered from the most important regions of North-West of Romania. According to our results, HPV16 is the most common high-risk type, being met in more than 1/5th from our cases, the majority of them in women aged between 31 and 40 years old. Other high-risk HPV types found were 31, 33 and 58. Associations of 2 high-risk HPV types or associations between one high-risk type and the other one low-risk type were found in 15 cases. The prevalence of high-risk HPVs has increased among women from North-West region of Romania, so national HPV screening programme and vaccination need to continue.

Introduction

Human Papillomavirus (HPV) is the most common sexually transmitted disease worldwide. HPV causes the majority of the malignancies situated at the level of the cervix, but it can also produce malignancies of the anal region, vaginal region, malignancies of the vulva, of the oropharynx and of the penis [1]. According to WHO (World Health Organisation), latest data about the global incidence of cervical cancer show 660,000 new cases in 2022, of which almost 350,000 women died because of this condition [2]. Mean age for women who died because of cervical cancer is 59, with variations between 45 and 76 years old. In Romania, the incidence of cervical cancer is 20/100,000 women and mortality rate is high, with 5-10 deaths/ 100,000 women. In Europe, Romania occupies the 2nd place in cervical cancer, after Montenegro, as it is followed by Moldova, Bulgaria and Lituania [3,4].

Based on its pathogenicity, HPVs can be grouped in low-risk (LR) types HPV, high-risk (HR) types HPV and undetermined (UD) types [5]. Types 16, 18, 31, 33, 35, 39, 45, 52, 56, 58, 59, 66 and 68 are considered high-risk HPVs and types 6, 11, 28, 32, 42, 43, 44, 51, 61, 62, 70, 71, 72, 81, 83, 84, 86, 87 and 89 are considered low-risk HPVs [5-7]. The majority of HPVs are asymptomatic and they are eliminated within 12-24 months from the

onset of the infection [5]. Sometimes, some of the infections become persistent and they can lead to premalignant cervical lesions and, in the end, to cervical cancer [5]. HPV infection of the cervix (especially types 16 and 18) can cause premalignant lesions, being the primary cause of intraepithelial malignant lesions [5]. HPV 16 is the most carcinogenic type, responsible for approximately 50-60% of all malignancies of the cervix [5]. The second oncogenic type, capable of producing malignancies of the cervix, is HPV 18, responsible for approximately 10-15% of all cervical cancers [5]. Therefore, persistent infection with HPV types 16 and 18 is responsible for almost 70% of all cervical malignancies [5,8]. Risk factors such as smoking and immunocompromised patients lead to the persistence of HPV infection and increase the risk of developing cervical intraepithelial neoplasia [5].

In Romania there are screening national programmes for detection of HPV and for malignant and premalignant cervical lesions (Babeș Papanicolau), programmes which can reduce the incidence and prevalence of cervical cancer.

Worldwide, vaccines were implemented to reduce the risk of cervical cancer. In Romania, HPV vaccination regards children, both sexes, aged between 11 (starting vaccination from 9 years old is also possible) and 18 years old and women aged between 19 and 45 years old [9].

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Gardasil-9 vaccine covers 9 low-risk and high-risk types of HPV (6, 11- low-risk, and 16, 18, 31, 33, 45, 52, 58 - high risk), but, because it is not a part from National Vaccination Programme, it is not compulsory to be done [10].

Aim and objectives

The purpose of this study is to identify which types of HPV are more frequently met in females from North-West of Romania and to establish the distribution of HPV types among women, regarding the age.

Material and methods

To identify which type of HPV is met among women in North-West of Romania, the cases were collected from Resident Laboratory, Oradea, in a time interval between 01.01.2022 and 31.12.2022. The cases were gathered from the most important regions of Nord-West of Romania, like Bihor County, Sălaj County, Cluj County, etc. Inclusion criterion: all women ranged between 22 and 70 years old, coming from both urban and rural environment.

Samples for HPV were collected with the help of a brush which was inserted into the vagina, through a speculum, up to the cervix for cervical cells collections and cellular debris from the vaginal fornixes. For detection of HPV types, Real-Time Polymerase Chain Reaction (RT-PCR) system was used.

The data obtained were introduced in Microsoft Office Excell 2016 and the results were processed with the help of Statistical Package for Social Sciences, Version 26 (SPSS 26). All the data were labelled as being ordinal or nominal variables. The results were fulfilled through mean, median, crosstab, standard deviation, Pearson and Eta Coefficients.

Table 1. Distribution of women by age

		Frequency	Valid Percent
Valid cases	22-30	134	29.1 %
	31-40	170	37.0%
	41-50	96	20.9%
	51-60	37	8.0%
	>61	23	5.0%
	Total	460	100.0%
Mean		38	
Median		36	
St. Deviation		10.55693	

Table 2. Distribution of HPV in the examined samples

HPV positive/negative			
		Frequency	Percent
Valid cases	inconclusive	2	0.4%
	negative	270	58.7%
	positive	188	40.9%
	Total	460	100.0%

Results

Between 01.01.2022 and 31.12.2022, 460 women enrolled for HPV determinations, the lower age limit being 22 years old and the upper age limit being 70 years old, with a mean age of 38. The majority of women were aged between 31 and 40 years old, followed by 22-30 years old females (Table 1). At the opposite end are women over 61 years old.

In more than 1/3 of all cases HPV was detected, but Pearson correlation coefficient situated very close to 0 indicates that there is no statistically significant relationship between the HPV test result (positive/negative/inconclusive) and age (Tables 2 & 3).

Regarding the high-risk HPV, according to our results, HPV 16 is the most common type, being met in more than 1/5th from our cases, the majority of them in women aged between 31 and 40 years old. Other high-risk HPV types found in women from North-West of Romania were 31, 33 and 58. Associations of 2 high-risk (HR) (16, 18 HR, or 16, 31 HR) types or associations between one high-risk type and the other one low-risk type were found in 15 cases. Additionally, combinations of 3 types, including compulsory one high-risk type, were found in 6 cases. Low risk HPV types were also noticed, HPV6 being most commonly met, followed by HPV54, HPV70 and HPV83. Associations of two low risk HPV types were also found (Table 4). However, beside low-risk and high-risk HPV types, undetermined HPVs was noticed like types 53 and 66, gathering more than 10% from all the cases. According to our results, high-risk HPV types were noticed in 64% from all positive HPV cases, meaning that the high-risk HPV incidence among women of North-West of Romania is more than 25%.

Table 3. Person Coefficient correlation between HPV and age decades

		Age decades	HPV Positive/ Negative/ Inconclusive
Age decade	Pearson Correlation	1	-0.077
	Sig. (2-tailed)		0.101
	N	460	460
HPV Pos/Neg/Inc	Pearson Correlation	-0.077	1
	Sig. (2-tailed)	0.101	
	N	460	460

We used Eta Coefficient to establish if there is any correlation between high-risk HPV16 and the age of women. Because of an Eta Coefficient situated under 0.2 (0.114) we admitted that there is no statistical significance between age and HPV16, so this high-risk type of HPV can be found in both young and old women, ranged between 22 and 64 years old (Table 5).

Discussions

HPV is an infection that occurs in both sexes, men and women, and when it becomes persistent it can lead to malignancies of the cervix, vagina, vulva, penis, anus and oropharynx [11-13]. In women, HPV is responsible for more than 95% of all malignancies of the cervix [2].

Table 4. Correlations between HPV types and age

						Age Decades	Total	
			22-30	31-40	41-50	51-60	>61	
HPV Type Total	16HR	Count	13	19	4	3	2	41
		% of Total	6.9%	10.1%	2.1%	1.6%	1.1%	21.8%
	16HR; 18HR	Count	1	0	0	0	0	1
		% of Total	0.5%	0.0%	0.0%	0.0%	0.0%	0.5%
	16HR; 31HR	Count	0	1	0	1	0	2
		% of Total	0.0%	0.5%	0.0%	0.5%	0.0%	1.1%
	18HR	Count	2	2	0	0	0	4
		% of Total	1.1%	1.1%	0.0%	0.0%	0.0%	2.1%
	2HR	Count	2	5	0	0	0	7
		% of Total	1.1%	2.7%	0.0%	0.0%	0.0%	3.7%
	3 combina- tions, 1 is HR	Count	1	2	3	0	0	6
		% of Total	0.5%	1.1%	1.6%	0.0%	0.0%	3.2%
	31HR	Count	4	6	0	0	0	10
		% of Total	2.1%	3.2%	0.0%	0.0%	0.0%	5.3%
	33HR	Count	1	4	3	1	0	9
		% of Total	0.5%	2.1%	1.6%	0.5%	0.0%	4.8%
	39HR	Count	0	2	0	0	0	2
		% of Total	0.0%	1.1%	0.0%	0.0%	0.0%	1.1%
	45HR	Count	0	3	1	0	0	4
		% of Total	0.0%	1.6%	0.5%	0.0%	0.0%	2.1%
	52HR	Count	1	0	0	0	1	2
		% of Total	0.5%	0.0%	0.0%	0.0%	0.5%	1.1%
	53UD	Count	5	5	3	0	1	14
		% of Total	2.7%	2.7%	1.6%	0.0%	0.5%	7.4%
	54LR	Count	2	1	2	0	0	5
		% of Total	1.1%	0.5%	1.1%	0.0%	0.0%	2.7%
	58HR	Count	3	0	3	1	1	8
		% of Total	1.6%	0.0%	1.6%	0.5%	0.5%	4.3%
	59HR	Count	0	1	0	1	0	2
		% of Total	0.0%	0.5%	0.0%	0.5%	0.0%	1.1%
	61/72LR	Count	2	3	4	0	1	10
		% of Total	1.1%	1.6%	2.1%	0.0%	0.5%	5.3%
	66UD	Count	0	4	4	1	0	9
		% of Total	0.0%	2.1%	2.1%	0.5%	0.0%	4.8%
	6LR	Count	4	4	5	0	0	13
		% of Total	2.1%	2.1%	2.7%	0.0%	0.0%	6.9%
70LR	Count	3	1	0	0	0	4	
	% of Total	1.6%	0.5%	0.0%	0.0%	0.0%	2.1%	
83LR	Count	0	2	2	0	0	4	
	% of Total	0.0%	1.1%	1.1%	0.0%	0.0%	2.1%	
Other HR	Count	1	1	0	0	0	2	
	% of Total	0.5%	0.5%	0.0%	0.0%	0.0%	1.1%	
Other LR	Count	1	3	2	0	0	6	
	% of Total	0.5%	1.6%	1.1%	0.0%	0.0%	3.2%	

			22-30	31-40	41-50	51-60	Age Decades	Total
							>61	
LR and HR	Count		3	7	1	1	0	12
	% of Total		1.6%	3.7%	0.5%	0.5%	0.0%	6.4%
UD and HR	Count		3	5	0	0	0	8
	% of Total		1.6%	2.7%	0.0%	0.0%	0.0%	4.3%
UD and LR	Count		2	0	0	1	0	3
	% of Total		1.1%	0.0%	0.0%	0.5%	0.0%	1.6%
		Count	54	81	37	10	6	188
		% of Total	28.7%	43.1%	19.7%	5.3%	3.2%	100.0%

Table 5. Eta Coefficient correlations between age and HPV type

Nominal by Interval	Eta	Value
	HPV16 Dependent	0.801
	Age Dependent	0.114

Ilisiu et al. showed in a study the presence of HPV among women from Romania aged between 18 and 70 years old (14). The study that we conducted showed similar results, with a mean age of 38 in women ranged between 22 and 70 years old, even if the age lower limit is slightly higher compared with other national and worldwide studies [9,14,15]. The prevalence of HPV is highest among sexual active women and decrease in older women [16].

According to World Health Organisation, global prevalence of HPV in women is 12%, with the highest rate of 24% in Africa, followed by Latin America (16%) and by Eastern Europe with 14% [17]. HPV testing resulted positive in more than 40% from our cases. This result is almost three times higher compared with the incidence of HPV in Eastern Europe. At the national level, the prevalence of HPV increased over time, being twice higher compared to other previous national scientific reports [14].

HPV infections are usually limited and they clear naturally in several months [18]. However HPV16 and HPV18 are highly oncogenic types, they produce epithelial proliferation so they are responsible for more than 70% of all cervical malignancies. Our study revealed that indeed HPV16 is the most common type met in North-West of Romania, in young, sexually active women. Based on our results, HPV18 is less common in Romanian females compared with females from others countries [19,20]. However, the incidence for high risk HPV31, HPV33 and HPV58 is lower in North-West of Romania compared with other countries [21].

These results lead us to consider that continuation of HPV screening programmes, appropriate treatment and patient follow-up are very important in this domain. For early diagnostic and for curative treatment national screening programmes are essential, a single screening being capable of decreasing the incidence and mortality of cervical malignancies [10]. Nowadays, in Romania, screening programmes are free of charge for women aged between 24 and 64 years old. Screening programmes are proved to be very useful tools in decreasing mortality and incidence of cervical malignancies with 42-92% in Europe [22]. However, when compare mortality rate of Romania because of cervical cancer mortality of all Europe, Romania still has a three times higher mortality rate (18%) because of this condition.

Romania is still dealing with lack of health education among the population, so we consider necessary to provide more detailed information to population about HPV and about the malignant lesions that HPV is able to produce. Also, a more agresive publicity in terms of screening and vaccination programmes of HPV needs to be conducted.

The limitations of the study consist in the fact that the studied group refers to just a part of the female population of North-West of Romania, because the data used were gathered from a private laboratory and not from all private and public health servicies of the region. Further investigation in this domain will be done, by colecting data from all regional laboratories in order to expand the study to all women from north-west part of the country.

HPV-related cervical cancer is a condition that could be almost completely eradicated through vaccination programmes for children and adolescents, along with public health and sexual education and lifestyle changes.

Conclusions

Cervical malignancy associated to HPV infection is still a national health problem, cervical cancer mortality being three times higher in Romania, compared with the rest of the Europe. According to our results, in the last few years the prevalence of high-risk HPVs has increased among women from North-West part of the country and the majority of the females most exposed to the infection remain young, sexually active ones. The conclusions of our report show the desperate need for continuing the national HPV screening programme and vaccination among women from Romania.

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