

Human Papillomavirus Infection and Awareness of Human Papillomavirus Vaccines among Various Ethnicities in Libya

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Abstract

Background: Human papillomavirus (HPV) plays a role in increasing the risk of cervical cancer and other cancers. This study aimed to explore the incidence of HPV infection among various ethnicities in Libya. Furthermore, awareness and knowledge of HPV vaccines in the community were explored.

Methods: A descriptive study was conducted to present HPV infection among cancer cases using the National Cancer Registry of Libya year 2011–2020, including gender, skin color, and ethnicity. Furthermore, awareness and knowledge of the HPV vaccines were assessed using questionnaires distributed through social media. Data were presented in percentage.

Results: In total, there were 33,526 (58.1%) infected HPV-related cancers out of 57,620 cancer cases, of whom 25,296 (75.4%) were women and 8,230 (24.6%) were men. Based on cancer sites, the incidence of HPV-related cancers among whites was higher (>63% and more) than blacks except for anal cancer, of which blacks had a slightly higher incidence (54% in females and 57% in males). Based on ethnicity, native Libyans such as Tabu, Touareg, and Berbers had different cancer sites. Moreover, the knowledge and awareness about HPV and related cancers were very poor among the population in Libya.

Conclusions: Although HPV cancers represent a high percentage of cancer burdens among Libyans, awareness and knowledge on HPV and related cancer are lacking. Better education and provision of the HPV vaccines for future generations may eliminate and reduce HPV-related cancers.

Keywords: Anal cancer, cervical cancer, HPV, Libya, sexually transmitted disease

Introduction

Human papillomavirus (HPV) is a common sexually transmitted virus, infecting most women and men during their lives. Based on the cancer potential, viruses are classified into high risk and low risk.^{1,2} In many cases, infection with the HPV occurs without the appearance of any symptoms. However, HPV infection may develop in various types of cancer in some women and men, in accordance with the target organ. About 70% of HPV-16 and HPV-18 are at high risk of causing cervical cancer (CC), in addition to a subset of genital anal cancer especially in the vagina, vulva, anus, penis, and pharyngeal cancers.^{3,4} Currently, there are three HPV vaccines

available in the global market, that are highly effective against various HPV genotypes.⁵⁻⁹ The bivalent vaccine covers HPV-16 and HPV-18; whereas the quadrivalent vaccine covers also low-risk HPV-6 and HPV-11, next to the high-risk HPV-16 and HPV-18. Moreover, five other extra high-risk genotypes of the nonavalent vaccines have been added, including HPV-31, HPV-33, HPV-45, HPV-52, and HPV-58. The protection against HPV infection is about nine years and a minimum of twenty years for high antibody concentration levels.¹⁰

Many countries have started HPV vaccination programs, right after the introduction of HPV vaccines. For example, Mexico had adopted the first quadrivalent HPV vaccine in 2006. The World Health

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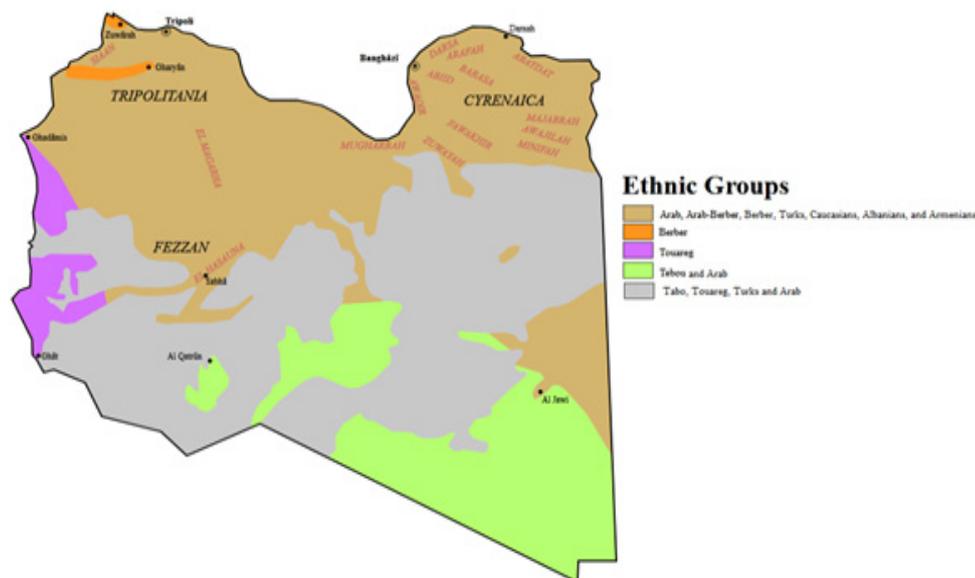


Figure Libyan Country and Dominant Ethnic Groups

Organization (WHO) had finally recommended routine vaccination against HPV in 2009. The actual effectiveness of HPV vaccines has become increasingly evident in countries with high vaccine absorption, especially in young women before exposure to HPV.¹¹ At the population level, the effects of vaccination against HPV decrease the HPV prevalence, cellular abnormalities in the cervix, and genital warts (GWs).^{12,13} The Committee on Immunization Practices (CIP) recommends that the vaccine should be administered routinely to females and males aged between 11 and 12; however, a study in this age group is limited.^{14,15} This study aimed to determine the prevalence of HPV infected cases in developing various cancers in Libya in the past decade. Furthermore, knowledge of HPV vaccines in the community was explored, hoping to educate various ethnicities in Libya about different types of HPV infection in women and men, and awareness of vaccinations against HPV.

Methods

This descriptive study had used nationally representative data from the National Cancer Registry of Libya year 2011–2020, predominantly from the national hospital's medical records. The incidence of HPV infection-associated cancer was stratified by gender, skin color, and ethnicity. As for ethnicity, the African native people in Libya

were Tabu, Touareg, and Berbers; the Asian was mostly Arabs; the European were Turks, Caucasians, Albanians, and Armenians as shown in Figure. Since this investigation used secondary data freely available in the public domain where there was no mentioning of the sample identity, ethical approval was unnecessary.

To assess HPV knowledge and vaccine in the community, Twitter and Facebook were used to recruit participants. A short validated questionnaire was distributed between 2019 and 2020 to explore the extent of citizens' education and knowledge of vaccines against papillomavirus. The data was anonymously gathered, therefore, ethical approval was not required. Data was further presented in percentage.

Results

The total subjects registered HPV infections in the National Registry from 2011 to 2020 were 57,620, including 72.8% cancer in females and 27.2% in males. Furthermore, infected HPV-related cancers was found in 33,526 (58.1%) of whom 75.4% (n=25,296) were females and 24.6% (n=8,230) were males (Table 1).

Although there was variation in the exact number of HPV-related cancers in Libya, data confirmed that HPV was associated with most cancers in the genital area, accounting for 60% and 52%, respectively, among females and males. Of those HPV infection cases in women,

Table 1 Incidence of Human Papillomavirus-related Cancers Based on Infected Organ Site, Stratified by Gender in Libya from 2011 to 2020

Gender	Total All	Cancer Site	Cases (n)	(%)	(%)***		
Female	-All HPV-related cancers		25,296	60*			
		Ovaries	9,264		36		
		Cervix	8,786		35		
		Anus	3,968		16		
		Vulva	1,697		7		
		Oropharynx	952		4		
		Vagina	629		2		
	-Other cancer		16,638	40*			
	Total female		41,934	72.8**			
Male	-All HPV-related cancers		8,230	52*			
		Oropharynx	4,115		50		
		Anus	2,971		36		
		Penis	1,144		14		
			-Other cancer		7,456	48*	
			Total male		15,686	27.2**	
			TOTAL		57,620	100**	

Note. *percentage in total females (n=41,934) or males (n=15,686); **percentage of all HPV related cancers and other cancer (n=57,620); ***percentage in cancer site for all HPV related cancers in female (n=25,296) or males (n=8,230).

ovarian (36%) and cervical cancer (CC; 35%) alone represented predominantly of all HPV-related cancers; whereas pharyngeal cancer accounted for 4%. On the contrary, oropharynx cancer in men accounted for 50% of total HPV-related cancer (Table 1).

HPV-related cancers affected ethnic groups to varying degrees. Generally, rates of HPV-associated cancers in whites (85%) were higher than in blacks (15%). Based on the cancer site, the incidence of HPV-related cancers among whites was higher (>63% and more) than among blacks, except for anal cancer, where blacks had a slightly higher incidence (54% in females and 57% in males) (Table 2).

Furthermore, stratifying by tribes, the incidence among natives, especially among Tabu (1%) and Touareg (2%), were considered consistently low, whereas the native Berbers were high (33%) similarly to Arabs (37%) and of European origin (27%). In gender stratification within ethnicity; ethnic differences were for some types of HPV-related cancers in which whites (85%) had a high incidence of pharyngeal cancer (77% females, 96% males). Among women, whites had the highest incidence of ovary cancer (83%) and vulvar cancer (85%). Tribes of Tabu, Touareg, and Berbers had consistently lower rates (Table 2).

In a parallel study, a total of 300 respondents had completed the questionnaire, of whom only 0.125% were aware of and knew about the HPV vaccination (Table 3). Furthermore,

the acceptability of HPV vaccination was explored, resulting in 63% who were willing to be vaccinated, whereas the other 37% were a negative their attitude regarding the vaccine. Those unwilling to be vaccinated believed that they had no risk of developing HPV infection, genital warts, or even cervical cancer or other cancers. Other 17% were worried that there was no use of the HPV vaccine in Libya. Respondents concerned with the safety and the efficacy of HPV vaccination accounted for 20%, participants who questioned the source of the vaccine and showed concern regarding the high price of the vaccine were 63%. More than 83% of participants agreed on educating the community about HPV infection and vaccines.

Discussion

Our study provided an important source of baseline data for HPV-related cancers in Libya in the last decade 2011–2020. There were 58.1% infected HPV-related cancers of total 57,620 cancer cases in the National Cancer Registry, which predominantly (75.4%) affect women. Through this report, it is advised to improve awareness of the HPV vaccine and to reduce the burden of HPV-related cancers and diseases. Currently, approval by the Libyan Ministry of Health and the Libyan government to adopt the HPV vaccine is awaiting. Vaccination against HPV may reduce the incidence of HPV-related cancers and precancerous lesions in Libya, therefore,

Table 2 Incidence of HPV-related Cancers Sites by Ethnicities and Gender in Libya from 2011 to 2020

Cancer Site	Skin color				Ethnicity									
	Black		White		Native						Asian Origin (Arabs)		European Origin	
	n	%	n	%	Tabu		Berber		Touareg		n	%	n	%
					n	%	n	%	n	%				
HPV-related cancers in female:	1,773	15	9,869	85	49	1	1,452	33	105	2	1,648	37	1,200	27
Ovary	1,110	17	5,356	83	745	27	347	12	201	7	725	26	780	28
Cervix	1,463	37	2,532	63	965	20	844	18	796	16	1,140	24	1,046	22
Anus	1,801	54	1,561	46	85	13	45	7	13	2	244	39	243	39
Vagina	117	25	351	75	65	40	17	10	9	6	59	37	11	7
Vulva	198	15	1,089	85	113	28	34	8	27	7	165	40	71	17
Oropharynx	123	23	421	77	35	8	15	4	12	3	123	30	223	55
HPV-related cancers in male:	814	16	4,390	84	126	6	215	10	0	0	928	42	907	42
Penis	109	11	880	89	89	15	2	0	2	0	287	46	245	39
Anus	951	57	730	43	170	15	161	14	10	1	330	28	480	42
Oropharynx	129	4	2,987	96	32	3	211	21	154	16	229	23	372	37

Note: Color skin is divided into Black and White. Ethnicity is divided by Native (Tabu, Berbers, Touareg); Asian origin (Arabs: Yemenite Gulf, Levant, and Iraq); European origin (Turks, Caucasians, Albanians, and Armenians).

initial responses to the HPV vaccination within the Libya public are favorable.

Not surprisingly, it sparked debate about data on HPV and related cancers in men and women, suggesting that HPV infection contributed to anal, penile, pharyngeal, and other cancers; given the specific link between HPV and penile, anal and pharyngeal cancer found in men who had sex with men. The incidence of cancer-related HPV infection is high among Libyan women. The rate of anal cancer is higher in men, about 36%; while the pharyngeal or oropharynx cancer rate is about 50% higher. For all combinations of HPV and penile-related sites, the rate is in the 14% range (Table 1). The incidence of hypopharyngeal cancer among men is two times higher than that of women.

Interestingly, the increased incidence of men might be due to several factors, including smoking and alcohol use which are both responsible for hypopharyngeal cancer.^{16,17} Furthermore, the cancer rate might be high due to sexual behavior and unhealthy diets. However, the pattern of HPV-associated cancers seemed to affect men only. As for cervical and ovarian cancer in women, which have higher rates, sexual behavior and genetic factors might be the predominant risk

factors. The results have shown that men are more susceptible to pharyngeal cancer for several reasons and factors, including HPV and smoking, alcoholic beverages, and drugs. Moreover, blacks have a high incidence of anal cancer (47% females, 57% males) and Europeans (42%), while Arabs (46%), and Europeans (39%) have a high incidence of penile cancer.

All HPV-related cancers have covered nearly all types of cervical cancer and some types of cancers of the vulva, vagina, penis, anus, and pharynx. As for the pharynx, HPV might infect the back of the throat, base of the tongue, and tonsils. Interestingly, the medical records noted that there were patients with two or more types of genital cancers such as ovarian and uterine cancer, or otherwise with another site such as colorectal and ovarian cancer at the same time. Moreover, there were those afflicted with two types such as uterine, renal cell carcinoma (RCC) and cancer of unknown primary (CUP); also, ovarian and CUP, Non-Hodgkin lymphoma (NHL) and cervix cancer; otherwise, vagina and cervix; bladder, ovary, cervix cancers; (ovarian, gastrointestinal cancer and CUP; CA-125 ovarian and uterine; Rectal cancer, colon cancer, ovary), and others. We did not find the explanation for these cases,

Table 3 Knowledge and Awareness around HPV and HPV Vaccine

Knowledge Statement	Answer				Gender			
	Know		Do not know		Female		Male	
	n	%	n	%	n	%	n	%
History of Papillomavirus (HPV) related lesions	-	-	300	100	-	-	-	-
HPV infection is widespread	-	-	-	-	300	100	-	-
HPV can cause serious diseases	-	-	300	100	-	-	-	-
HPV can infect both genders	4	1	296	96	1	-	3	-
Most HPV infected people develop cancer	3	1	297	97	1	-	2	-
HPV can lead to genital warts (GWs)	-	-	300	100	-	-	-	-
GWs affect both genders	-	-	300	100	-	-	-	-
HPV-related with penile cancer	-	-	300	100	-	-	-	-
HPV-related with CC	-	-	300	100	-	-	-	-
HPV infection transmission through sexual intercourse	-	-	300	100	-	-	-	-
Early sexual debut increases the risk of contracting HPV	-	-	300	100	-	-	-	-
Using condoms reduces the risk of HPV transmission	-	-	300	100	-	-	-	-
A high number of sexual partners increases the risk of contracting HPV	-	-	300	100	-	-	-	-
HPV infection transmitted from mother to child during pregnancy and delivery	1	1	299	100	1	-	-	-
HPV infection transmission from a carrier to his/her partner only if the carrier shows symptoms	-	-	300	100	-	-	-	-
A person may be HPV-infected and is unaware	5	2	295	97	-	-	3	1
There are no specific therapies for HPV infection	-	-	300	100	-	-	-	-
Heard about HPV vaccine	2	1	296	98	-	-	2	1
Anti-HPV vaccine is safe	1	1	299	100	-	-	1	-
Both genders can be vaccinated against HPV	2	1	298	99	1	-	1	-
HPV vaccine is effective after starting sexual activity	-	-	300	100	-	-	-	-
Anti-HPV vaccination must be mandatory for boys and girls before the sexual debut and for at risk subjects	-	-	300	100	-	-	-	-
Ages recommended the vaccines between 9 to 12	-	-	300	100	-	-	-	-
Anti-HPV vaccines are capable of preventing the occurrence of CC and GWs	3	1	297	97	1	-	2	-
Total %	0.125	-	99.875	-	-	-	-	-

as it was unknown why cancer appeared in two or more genitals and other organs in the same patient. Perhaps, there was a link between several factors such as early marriage, sexual disorder, reproduction, frequent miscarriages,

early sexual life, diet, race, and homosexuals with two or more sex partners. To hypothesize, this may occur due to an interaction between environmental and genetic factors, leading to abnormal gene expression and HPV infection.

Thus, functional changes to oncogenes play a significant role in the occurrence and evolution of HPV-16 and HPV-18 rates associated with rates of estrogen receptor (ER), progesterone receptor (PR), Tumor protein P53, and KI67 infection.

Moreover, HPV also destroys the normal sex hormone function, which weakens the anti-estrogenic effect of progesterone in the organs and increases the malignant transformation of cells. HPV may induce cell cycle activity of KI67 positive cells; as the expression level of KI67 increases, the numbers of copies of HPV also increase. There is no logical explanation for having multiple carcinomas in different organs of the same person.

Based on the cancer site, the incidence of HPV-related cancers among whites was higher (>63% and more) compared to blacks, except in anal cancer, of which blacks had a slightly higher incidence (54% in females and 57% in males). Oropharynx cancer was higher in white men (96%) than in white women (77%). Based on ethnicity, native Libyans such as Tabu, Touareg, and Berbers had different cancer sites.

The challenge of this study was the community's awareness of HPV-related cancers and vaccines against HPV. The knowledge and awareness of HPV and related cancer were inadequate among the population in Libya. Libyan-born Tabu and Berbers had the lowest HPV positivity in fewer HPV risk behaviors, including early age at first sexual intercourse, multiple sexual partnerships, and current smoking. The congruent genotypes and the biological factor might be responsible for HPV infection, and prevention of HPV depended on the awareness and promotion of vaccines against HPV and the number of doses allowed according to types of HPV vaccination. In high-risk HPVs, viruses that have a high possibility to develop cancer, include genotype HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59; of which two genotypes are the most prevalent, which are genotype HPV 16 and 18, causing the majority of HPV-linked cancers.^{14,15} There are vaccines for HPV available, which cover high-risk HPV genotype 16 and 18 (2-valent), and another one also covers low-risk HPV genotype 6 and 11 (4-valent). Genital warts, predominantly caused by low-risk HPV genotype 6 and 11, are not carcinogenic. Recently, the 9-valent (Gardasil 9) vaccine is available consisting of 9 genotypes HPVs (6, 11, 16, 18, 31, 33, 45, 52, and 58).¹⁸ A two-dose series of HPV vaccines for both genders should be given as early as nine years.¹⁹ In addition, a

three-dose series may be given to those who start the vaccine series at age 15 or older, and to people with certain weakened immunity. Vaccination against HPV is also recommended up to 26 years for women and 21 years for men who have not received adequate vaccinations.

Thus, adolescents should be vaccinated before exposure to HPV infection or be sexually active. Interestingly, most women under the age of 30 can self-clear HPV infection on their own within a few months or years. The vaccine will not eliminate HPV infection. Besides, the vaccine does not protect against all types of HPV, therefore, even women who are already vaccinated, still need to have regular Pap and pelvic exams, as the vaccine's effectiveness is not known yet.

There is a lack of knowledge and awareness of HPV infection and vaccines, therefore, educational initiatives are essential. The importance of organized enlightenment for health care workers and the media, who are the most preferred sources of information, is imperative. Due to the low knowledge level, the media and health professional promotion need to raise awareness.

This study used secondary data, so it faced several limitations, among others; the data was not supported by the age of the respondents. A better database in age groups could further support cancer management as cancer-related HPV infection was significant among different age groups.

To conclude, HPV-related cancer has infected 60% of women and 52% of men. Ovarian and cervical cancers in women are the predominant cases, and the oropharynx and anal are more prevalent in men. Although HPV cancers represent a high percentage of the cancer burden among Libyans, knowledge and awareness on HPV and related cancers are lacking. Better education and provision of HPV vaccines for future generations may eliminate and reduce HPV-related cancers. Furthermore, due to low knowledge levels, media and the promotion of health professionals must raise community awareness.

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