

## HPV Prevalence and HPV Related Disease in China and Jordan

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**Abstract: Objective:** To review and compare the common HPV infection genotypes in Jordanian and Chinese patients of different HPV related diseases, so we can get better understanding of HPV prevalence and its related cancers in China and Jordan.

**Method:** the data of HPV and its related disease are obtained from online resources such as PubMed, googlescolars and IARC (international agency for research on cancer).

**Results:** the cervical Crude incidence rates per 100,000 was (9,4) in China and (1.6) in Jordan, the head and neck cancers Crude incidence rates per 100,000 was 0.6 in Chinese males, 0.1 in Jordanian males, while for females in both countries, 0.2 for Chinese females and 0.0 in Jordanian females, the other anogenital cancers (anal, valvar, vaginal, penile) in china were 0.7 and 0.6 in Jordan. Most common HR-HPV genotypes in Jordan and China are HPV16,18,31,33,35,39,45,51,52,58,56,58,59,68,73,82, and LR-HPV include 11,6,42,44,55.

**Conclusion:** China have higher incidence rate of cervical cancer, head and neck cancers, and other anogenital cancers (anal, valvar, vaginal, penile), the prevalence of HPV infection are higher in China too, HPV 16 and 18 are the most common genotypes in Jordan, HPV 16 was the most common genotype in china but second position were between these three genotypes 53,58,18 in different lesion.

Jordan and China are placed in different territory in Asia; meanwhile, economic conditions, religion, cultural habits, population, and different risk factors have made difference in HPV infection prevalence, and the prevalence of different genotype of the cancers reviewed in the research above, in both countries

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### I. Introduction

Human papilloma viruses (HPV) is a group of non-enveloped DNA viruses. more than 200 types of HPV have identified to date, HPV can be categorized into either cutaneous and mucosotropic type, only 40 types can spread sexually and cause genital warts [1-4].

In general, 200 HPVs subtypes can be divided into High-Risk HPV and Low-risk HPV, that most of these 200 subtypes are Low-risk HPV [5].

HR-HPVs have a high carcinogenic impact, High-Risk HPV are responsible for most of cervical cancers cases and a fraction of Head and neck cancer cases and other anogenital cancers too, such as anal, penile, vulvar, vaginal cancers cases. In contrast, Low-Risk HPV have a low carcinogenic impact, that LR-HPV can cause self-limiting, asymptomatic lesions, which can be cleared by host self-immunity in most of the cases. Actually, LR-HPV can cause lesions include respiratory papillomatosis and epidermodysplasia verruciformis, these lesions can be recurrent and refractory to treatment, and can be associated with cancer sometimes [5].

In the period between 1990 to 2000, epidemiological studies provided temporal evidence, that exposure to human papillomavirus (HPV) infections have a relation with the development of cervical cancer. Later on, HPV has become the first ever identified, "necessary cause" of a human cancer. This implies that cervical cancer can't develop in the absence of the persistent presence of HPV infection [6]. That in year 2008, ZurHausen won the Nobel Prize in Physiology or Medicine for his discovery that linked HPV with cervical cancer.

HPV is responsible of 4.5% of all new cancer cases worldwide [7]. Every year 530,000 new cases of cervical cancer in the world [2].

The persistent High-risk HPV genotypes infections are responsible for cervical cancer [8], that genotypes 16 and 18 alone, approximately responsible for 70% of cervical cancers worldwide [9]. other common genotypes are 52,58,39,35,33,31,45,51,56,59,68,73,82[10]. Low-risk HPVs such as genotypes 11 and 6 can cause genital warts and respiratory papilloma, but rarely can develop to cancer [11].

HPV is one of the most common sexually transmitted disease (STD) worldwide, that it is the most common STD in the United State [12-14]. In addition to cervical cancer, HPV can cause many cancers, such as anal, penile, vaginal, vulvar cancers [15,16], That it was first noticed in 1935 by Rous and beard.

Cervical are caused only by HPV, meanwhile the OPC etiology can be one of two: tobacco and alcohol consumption or HPV infections [17]. Epidemiological shift in many western countries OPC , that the classic OPC patient used to be alcoholic, smoker, old males. While now HPV related OPC prevalence are getting higher than before, that in the United State in the period between 1988-2004, HPV related OPC incidence increased 225% and expected to be more prevalent than cervical cancer in 2020 [18], this epidemiological shift rise a new term called the ‘new’ OPC patients, whom are young, educated, high socioeconomic status and non-smoker or alcoholic [19, 20].

Cervical cancer screening methods have decreased the incidence and mortality of cervical cancer, but the benefit of these screening methods isn’t fully reached in developing or developed countries, that in developing countries the benefit are low due to having poorly organized screening program, and in developed countries benefits are not maximized due to the cost, anxiety, discomfort during the procedure and sometimes access problems. All that result into poor outcome from cervical cancer [21-25].

The aim of this study is to review and compare HPV genotype prevalence, and HPV related cancers in China and Jordan, comparing the two countries prevalent HPV genotypes may help us to understand HPV distribution in both countries, and setup plans for controlling this growing infection in Jordan, china.

## II. Method and materials:

### Data Sources

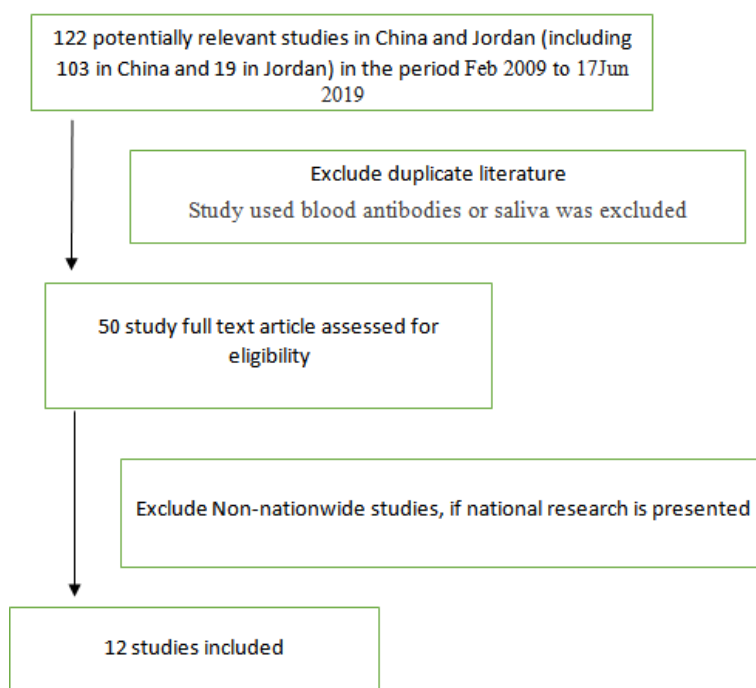
Data in this surveillance are obtained from online published data, websites such as PubMed, googlescolars, IARC (international agency for research on cancer) which is international organization in France, Paris that it makes an annual HPV and it is related disease’s report for many country’s including China and Jordan.

The Inclusion criteria was any research of HPV prevalence or HPV related disease and its HPV genotype prevalence in Jordan and china.

The Exclusion criteria was any research are not national research in china, meaning any research not done in many representative cities of china, because of the big population and large area of china, but in Jordan due to the small population and small area, no need to exclude research not done on whole national level, because situation is similar in each city, due to the patient seek medical care in different cities of the country frequently.

### Search strategy

Thearticles and reports included in this descriptive review (figure 1) study are the articles of HPV genotypes prevalence or HPV related diseaseprevalence in Jordan and china from the period Feb 2009 to 17Jun 2019.



**III. Results**

A total of 126 article were retrieved to the search strategy above (figure 1), 103 articles in China and 19 articles in Jordan, all articles duplicates or studies not done in nationwide level in case national research is present were excluded, after exclusion of noneligible studies only 12 articles and reports were used in this review study.

**Cervical cancer**

According to IARC latest estimation of cervical cancer statistics was in year 2018, see Table (1). China had 106,430 new cases of cervical cancer, compared to 104 new cases reported in Jordan. China had a higher number of new cases than Jordan [26,37].

China had 15.4 crude incidence per 100,000, in compare to 2.1 crude incidence rate per 100,000 in Jordan, it is obvious China is having higher prevalence of cervical cancer than Jordan [26,27].

The estimation of Cervical cancer statistics by IARC before year 2018, was in year 2012. We can notice there is increase of annual new cases in the Chinese population, comparing years 2012 and 2018. That in 2018 the cervical cancer new cases reported increased by 44,739 new cases, comparing to 2012 year (61,691 new cases reported) [26,28].

Annual new cases in Jordan increased too, that only new 50 cases reported in 2012, while in year 2018, 106 new cases were reported, with increase of 54 new cases between years 2018 and 2012 (table 1) [28,29].

In 2012 61,691 new cases were reported in China. This number increased to be 106,430 new cases of cervical cancer in 2018 year. The number of Cervical cancer annual new cases increased 44,739 new cases in year 2018, compare to year 2012, see Figure (2) [26,28].

We can notice increase of cervical cancer in China and Jordan between the years 2012 and 2018 (Figure 2).

In year 2017 China cervical cancer incidence was 9.4, one year later (2018) incidence increased to be 15.4. The incidence in Jordan were 1.6 in year 2012, and in year 2018 cervical cancer incidence increased to be 2.1.

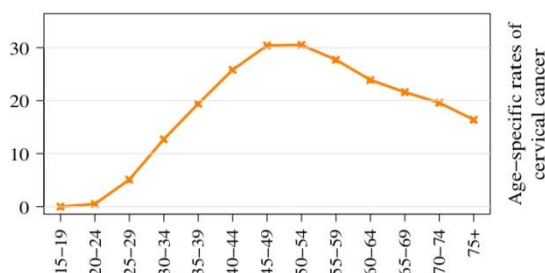
In general, cervical cancer incidence in last two estimation, for the years 2012, 2018 are higher in China, in compare to Jordan. that in 2012 China cervical cancer incidence were 6 folds higher than Jordan. In 2018 incidence in China became almost 7 folds higher than Jordan.

Last two estimation for incidence of cervical cancer, showed increasing of the incidence in both China and Jordan, the incidence of cervical cancer was doubled in 2018, in compare to 2012. Jordan cervical cancer incidence increased too, that in 2012 it was 1.6, and become 2.1 in 2018.

**Table (1): 2018 key statistics for cervical cancer in China and Jordan:**

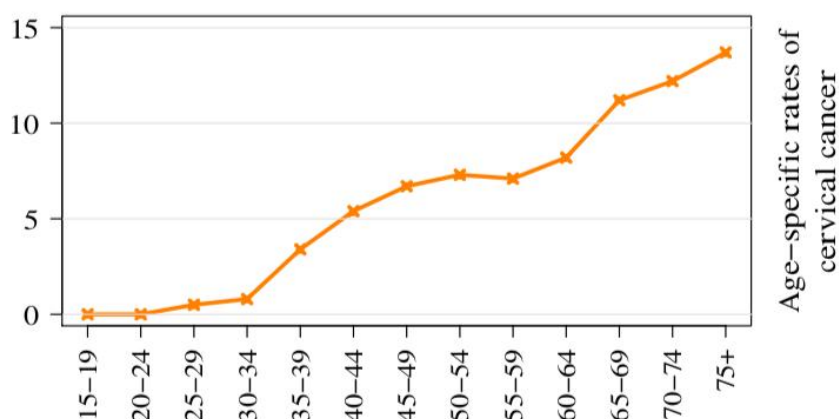
Numbers of HPV prevalence	Country	Jordan	China
Women at risk of cervical cancer		2.5 million	526.8 million
Number of new cervical cancer cases (2018 estimate)		104	106,340
Number of new cervical cancer cases (2012 estimate)		50	61,691 new cases
Crude incidence rate per 100,000 (2018 estimate)		2.1	15.4
Crude incidence rate per 100,000 (2012 estimate)		1.6	9.4
Annual number of cervical cancer death (2018 estimate)		61	47,739
Annual number of cervical cancer death (2012 estimate)		19	29,526

China age-specific rates of cervical cancer (figure 2A) that it begin to rise in earlier age, exactly after age of 24, and have a peak between age of 45-54, then the incidence decrease gradually, but Jordan (figure 1B) have a late age increase of incidence, which happen to be after age 34, then a steady gradual increasing of incidence with no any decrease happen again, in contrast China has decrease of incidence after the peak, between age 45-54, while both countries have most of the patients of cervical cancer between ages of 40-64 [26,27].



**Figure (2A): 2018yr Age specific of cervical cancer in China. reference [26] \*rates per 100,000**

\*15-19 yrs:15 case.20-24 yrs:219 cases.25-29yrs:2823 cases.30-34:7571cases.35-39 yrs:9038 cases.40-44yrs:13073 cases.45-49 yrs:18533 cases.50-54 yrs:17636 cases.55-59 yrs:12348 cases. 60-64 yrs:9180 cases.65+yrs:15994 cases.



**Figure (2B):** 2018yr Age specific of cervical cancer in Jordan. Reference [27] \*rates per 100,000 women per year

\*15-19 yrs:0 case.20-24 yrs:0 cases.25-29yrs:2 cases.30-34:3 cases.35-39 yrs:11 cases.40-44yrs:15 cases.45-49 yrs:16.50-54 yrs:14 cases.55-59 yrs:10 cases. 60-64 yrs:8 cases.65+yrs:25 cases.

**Head and neck cancers (Pharyngeal cancer excluding nasopharynx)**

In 2018yr, the number new cases of males in China were 4,227 new cases, while in Jordan 5 new cases were reported, obviously the number of new cases are more in china, the crude incidence rate per 100,000 were higher in China, that in Chinese males(0.6), six folds higher than in Jordanian males (0.1), meaning that the new cases in china are more not just due to the big population of china, but due to the higher incidence rate there too (table 2A)[26,27].

**Table (2A):** 2018 Head and neck cancer key statistics in Chinese and Jordanian males:

	Jordan	China
Annual number of new cancer cases	5	4,227
Crude incidence rate	0.1	0.6
Age-standardized incidence rate	0.2	0.1
Cumulative risk (%) at 75 years old	0.0	0.0

\*reference [26,27].

\*age-standardized incidence rate is the summary rate that would have been observed, given the schedule of age-specific rate, in a population with age composition of some reference population, often called the standard population.

\*cumulative risk (%) at 75 years old is the probability or risk of individual getting from the disease during ages 0-75.

\*rates per 100,000 males per year

In2018yr, the number new cases of females in China were 1,155 new cases, while in Jordan 2 new cases were reported, the crude incidence rate per 100,000 for Chinese females was (0.2), and (0.1) in Jordanian females.(table 2B) [26,27].

**Table (2B):** 2018 Head and neck cancer key statistics in Chinese and Jordanian females:

	Jordan	China
Annual number of new cancer cases	2	1,155
Crude incidence rate	0.1	0.2
Age-standardized incidence rate	0.2	0.4
Cumulative risk (%) at 75 years old	0	0

\*reference [26,27].

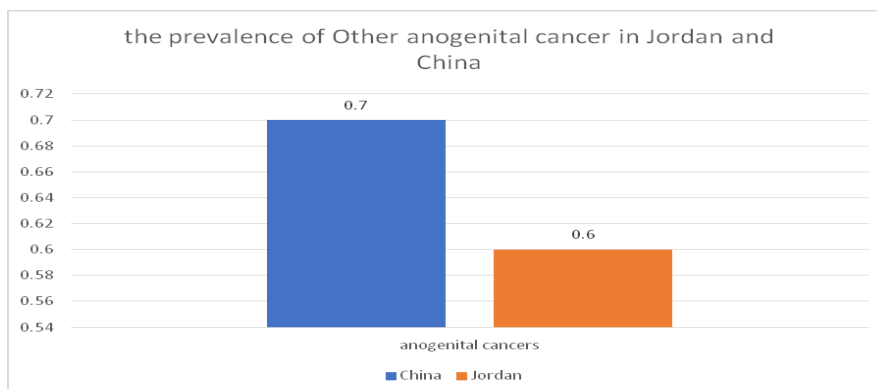
\*age-standardized incidence rate is the summary rate that would have been observed, given the schedule of age-specific rate, in a population with age composition of some reference population, often called the standard population.

\*cumulative risk (%) at 75 years old is the probability or risk of individual getting from the disease during ages 0-75.

\*rates per 100,000 males per year

**Other anogenital (penile, vulvar, vaginal, anal) cancers**

The prevalence of the other anogenital cancers are more in china (0.7 per 100,000) while in Jordan was (0.6 per 100,000), again China gets higher prevalence of HPV related cancers than Jordan, and this time China higher prevalence wasn't with big gap (figure 3) [26,27].



**Figure(3):** 2018yr prevalence of the other anogenital (penile, vulvar, vaginal, anal) cancers.reference [32,33].  
\*rates per 100,000 per year

**IV. HPV Genotypes Prevalence**

According to IARC (figure 4),cervical cancer lesionstop 10 most common Genotypes in China were 16,18,58,52,33,31,59,45,39,56 respectively, and in Jordan the top10 most common Genotypes were16,18,56,39,45,33,59,35,31,58 respectively.

HPV 16,18 are the most common genotypes of cervical cancer in China and Jordan. HPV58 was the 3<sup>rd</sup> common genotype in China and the 10<sup>th</sup> in Jordan. The 3<sup>rd</sup> common genotype in Jordan was genotype 56, the same genotype was the 10<sup>th</sup> in China. HPV52 were the 4<sup>th</sup> common genotype in China, but wasn't among Jordan 10 most common genotypes in cervical cancer lesions. HPV39 were the 4<sup>th</sup> common genotype inJordan and the 9<sup>th</sup> common genotypein China, HPV45 were 5<sup>th</sup> common genotype in Jordan and 8<sup>th</sup> common genotypein China. HPV33 were the 5<sup>th</sup> common genotype in China and the 6<sup>th</sup> in Jordan. HPV31 were 6<sup>th</sup> in China and 9<sup>th</sup> in Jordan, HPV59 were the 7<sup>th</sup> in China and Jordan, HPV 35 were the 8<sup>th</sup> common genotype in Jordan and wasn't in the list of China top 10 common genotypes in cervical cancer.

Squamous cell carcinoma lesionstop 10 most common genotypes in Chinawere 16,18,58,52,33,31,59,39,56,45, and no available data for this lesion in Jordan.

Adenocarcinoma lesions top 10 most common HPV genotypes in China were 16,18,52,58,59,39,68,45,33,31, and no available data for this lesion in Jordan.

The unspecified lesions China top 10 most common HPV Genotypes are 16,18, 58,52,59,33,31,45,39,66, and in Jordan the top10 most common Genotypes were 16,18,56,39,45,33,58,35,59,31.

HPV 16,18 are the most common genotypes of the unspecified lesions in China and Jordan, the third common genotype were HPV58 in China and HPV56 in Jordan. HPV39 were the 4<sup>th</sup> common genotype in Jordan and the 9<sup>th</sup> in China, HPV52 were the 4<sup>th</sup> common genotype in China, while it was absent among the top 10 common genotypes in Jordan for these unspecified lesions. HPV59 were the 5<sup>th</sup> common genotype in China and the 9<sup>th</sup> in Jordan, meanwhile HPV45 were the 5<sup>th</sup> common genotype in Jordan and 8<sup>th</sup> in China, HPV 33 were 6<sup>th</sup> common genotype in China and Jordan. HPV35 were the 8<sup>th</sup> common genotype in China, and wasn't present among the top 10 most common genotypes for this lesion in Jordan. HPV31 were the 7<sup>th</sup> common genotype in China and the 10<sup>th</sup> in Jordan, the 10<sup>th</sup> most common genotype in China were HPV66.

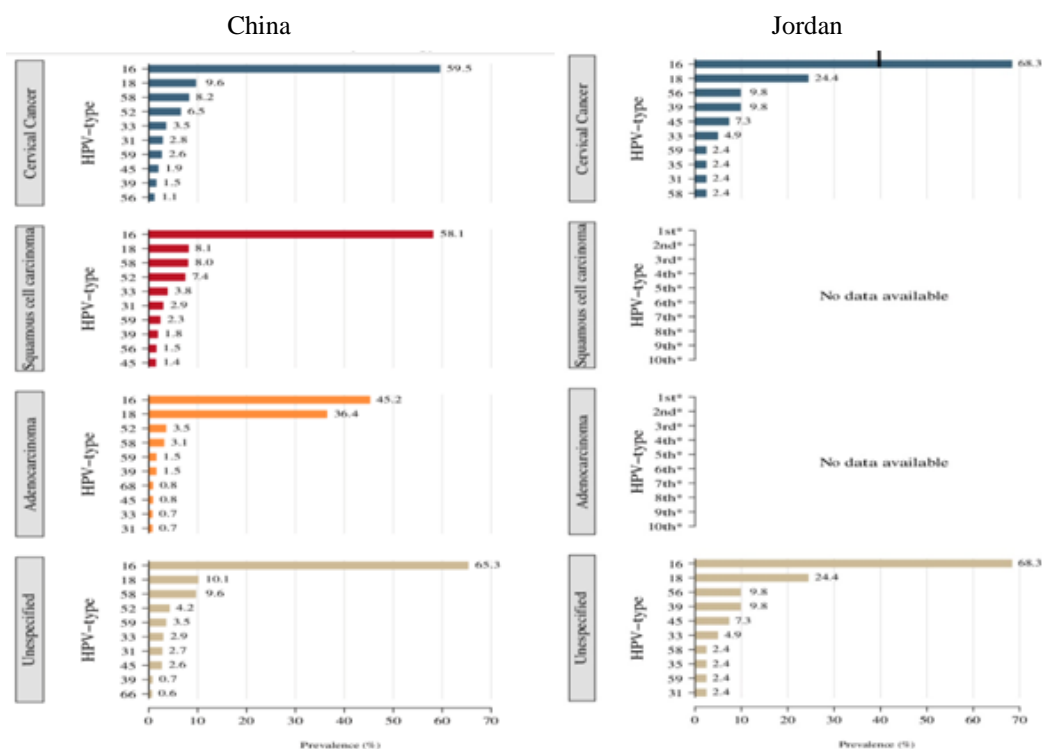


Figure (4): 2018 10 most common HPV genotypes among women with invasive cervical cancer by histology in China and Jordan. Reference 26,27.

\*rates per 100,000 women per year

## V. Discussion

This work compares the incidence of HPV related cancers, and different HPV genotypes prevalence in China and Jordan, also provide data for potential HPV vaccination and cancer screening program for the population at risk in China and Jordan.

### Cervical cancer

Persistent infection with High-risk HPVs in the female genital tract is one of the important causes of cervical cancer, making both Chinese and Jordanian females are at risk of this high prevalence cancer. The annual new cervical cancer cases are more in China in compare to Jordan, this result isn't just due to the bigger Chinese population, but due to the higher crude incidence rate in China too, the reason could be because HPV infection in cervical patients is different in different countries and in different regions [30] another cause can be the high rate of High risk-HPV infection in China 19% (95% CI) [31].

In the period between 2017 and 2018 both China and Jordan got increase of the of cervical cancer incidence, the number of new cases between 2017-2018 is almost the double in both counties. according to IARC, HPV vaccination and cervical cancer screening coverage are very low in both countries, this maybe explain the reason behind this big increase of cervical cancer incidence in China and Jordan [26,27,28,29].

The big difference of cultural, religion and regional factors between Jordan and China maybe stands behind the reason why cervical cancer prevalence is higher in China than Jordan.

### Head and neck cancer

Larynx cancer is the sixth most common cancer worldwide [15] and HPV is an important risk factor for head and neck cancers.

Big gap in the numbers of new cases and crude incidence for head and neck cancers between Chinese and Jordanian males, meaning China again have a higher incidence rate of this HPV related cancer, in compare to Jordan.

The incidence rate and annual new cases number gap between China and Jordan, can be due to many risk factors associated with head and neck cancers. Smoking and Alcohol drinking are associated with high rates of head and neck cancers.

HPV associated oral pharyngeal squamous cell carcinoma (OPSCC) in the United State, increased 225% between 1988-2004, and will surpass the incidence of cervical cancer in 2020 [32]. This epidemiologic change can be called as "new" head and neck cancer patient.

As we reviewed the risk factors of head and neck cancer culture, alcohol consumption, smoking, and sexual behavior could be causing the higher incidence in China. Other anogenital (penile, vulvar, vaginal, anal) cancers

China got higher incidence of these other anogenital cancers, discussing and comparing the incidence rate of each cancer of the other anogenital cancers alone are not possible, because the lack of data in Jordan, but we can still know the incidence rate of these anogenital cancers together are higher in China than in Jordan.

No big gap of prevalence between the two countries in the other anogenital cancers, leading to think that risk factor level of this type of HPV related cancers are somewhat similar in China and Jordan.

### HPV genotypes prevalence

Persistent infection with human papillomavirus (HPV) has been clearly established as the necessary cause of cervical cancer [33,34], at least 40 different HPV types are known to infect the genital mucosa, of which approximately 15 are associated with cervical cancer, among these types [1-4]. In Jordan HPV16 and 18 are the most common genotypes in Jordan in most of HPV related lesions and cancers, except for the normal cytology lesions.

HPV prevalence varies with the grades of cervical cancer and cervical precancerous lesions, that the incidence rate of genotypes 16 and 18 increases with the lesion malignancy grade getting higher, seeming that genotypes 16 and 18 have a high carcinogenic level in compare to the other HPV genotypes.

HPV infection in cervical patients is different in different countries and in different regions [30], that we can see HPV 16 and 18 are the two dominant genotypes in Jordan, meanwhile genotypes 16,53,58 are the most common genotypes in China.

Anal cancer is the most cancer strongly associated with HPV, yet much less is known of the natural history of anal cancer compared to cervical infection [35], but The Data of the common HPV genotypes prevalence in both countries are not enough to make the comparison yet.

## VI. Conclusion

Most significant findings of this study are as follows: (1) China has a higher prevalence of Cervical cancer, Head and neck cancers, and other genital cancers, in compare to Jordan. (2) HPV16 and 18 are the most prevalent genotypes in Jordan, and genotypes 16,52,58 are the three dominant genotypes in China (3) In the period between 2017 to 2018, cervical cancer prevalence is increased, in both Jordan and China. Meanwhile Cervical cancer screening coverage are low in both countries, HPV vaccination program in China began in the recent years, while no HPV vaccination program in Jordan, therefore attention should be paid to the prevalence of cervical cancer and HPV infections. This indicate urgently national plan, for a better cervical cancer screening program in China and Jordan.

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