Knowledge on Human Papillomavirus-Related Conditions and Determinants of HPV Vaccine Uptake for Cancer Prevention among Japanese University Students: Survey and Review

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Abstract

Objectives

Human papillomavirus (HPV) causes an infection that is related to nearly 99% of cervical cancer cases. The World health organization (WHO) estimates that there is an increase of 300 million HPV carriers per year worldwide. We evaluated the knowledge on HPV-related conditions, their prevention and HPV vaccine uptake among Japanese university students.

Methods

A survey was conducted in which 679 students (225 males and 454 females; mean age: 19.8 ± 6.17) from three universities (Kochi prefecture) participated. In addition, a review of the literature on HPV vaccination and cervical cancer in south-east Asia was performed.

Results

Twelve percent of female students were vaccinated. In total, 18% of participants had accurate knowledge on HPV-related illnesses; women (76%) had high knowledge as compared with their male counterparts (46%; p<0.05). When faculty was considered, nursing and medical students had high knowledge on HPV-related conditions than those from other faculties (p<0.05). HPV vaccine uptake was positively associated with 3 'having a close person (sibling, relative, acquaintance or friend) who suffered from cervical cancer (OR: 2.18; 95% CI: 1.31-3.63; p<0.05).

Conclusion

This study showed that, despite the relatively high incidence of cervical cancer in Japan, the rate of vaccine uptake was low. Controversy regarding safety of HPV vaccines in Japan should be addressed by health policy makers to eventually allow teenagers and young adult to get immunized.

Keywords: Cancer prevention; Determinant; Human papillomavirus; HPV vaccination; Student

Introduction

Human papillomavirus (HPV) causes a sexually transmitted infection that is responsible for approximately 99% of cervical cancer cases [1]. The World health organization (WHO) has reported an
increase of 300 million HPV carriers per year worldwide. Currently, there are approximately 100 HPV types, of which forty are reported to invade genital organs such as uterine cervix, vaginal wall and vulva in women, and penis in men [2-5]. A persistent infection of HPV type 16 and 18 is a 4 necessary cause of cervical cancer and risk factor of other epithelial-derived carcinomas 54 such as ano-genital and oropharyngeal cancer [4,6].

HPV vaccines have been proven to be highly efficacious in preventing HPV infection and precancerous cervical disease in randomized controlled trials [7], and it is suggested that universalization of HPV vaccination could markedly reduce the prevalence of HPV-related malignancies. In the US, vaccination is recommended for both boys and girls aged 11-12 years and women aged 13-26 years [8].

In Japan, the prevalence of HPV-infected pregnant women aged 20-29 years is high, 20-30% [9]. HPV vaccine was introduced after 2008 and was categorized as voluntary vaccine (to be paid by the beneficiary), and it has been recommended only for girls aged 9-14 years [10].

Given the paucity of information in regards to HPV awareness and vaccination coverage among Japanese young adults in the medical literature, we conducted a survey to evaluate the knowledge and awareness in regard to HPV-related conditions and determine the rate of HPV vaccine uptake in a sample of Japanese university students.

Materials and methods

Design and participants

A cross-sectional study was conducted in which students from five campuses of three Japanese public universities located in Kochi prefecture, Shikoku region, took part. After validation of the study questionnaire, 679 out of 827 participants (82%) answered and returned the questionnaire, including 225 males and 454 females (mean age: 19.8 ± 6.17). Male students were included in this Japanese study to verify the general opinion that males should not unnecessarily get vaccinated.

Survey questionnaire

The survey questionnaire (prepared in Japanese language by a collaborative multidisciplinary research team that included gynecologists) comprised socio-demographic information such as age, gender, place of permanent residence (hometown), university, grade, faculty/department, nationality, and 15 questions related to sexual behaviors, HPV and related illnesses and complications (HPV infection, genital warts and malignancies), history of HPV infection and genital cancer (personal, relatives, siblings or family members), preventive measures for HPV-related conditions and HPV vaccine uptake. Regarding HPV-related illnesses, a participant was considered as having accurate knowledge if he/she mentioned at least the following conditions: HPV infection/genital warts and malignancies (genital cancer such as cervical cancer, 88 non-genital cancers). On the other hand, a participant who recognizes the existence and 6 beneficial effects of HPV vaccines, which are proved to be efficacious against most prevalent HPV types, was considered to have good knowledge on the prevention of HPV-related illnesses.

Ethical consideration and statistical analysis

Informed consent was obtained from each participant and the study protocol was approved by the Social Medicine division of Kochi University Medical School, Japan. Data are expressed as proportions. To determine factors associated with HPV vaccine uptake, respondents were divided into two groups, according to their HPV immunization status, and a multivariate logistic regression analysis was performed. P-values less than 0.05 were considered statistically significant. All the analyses were performed with the use of Stata software version 10 (StataCorp, TX, USA).

Results

Characteristics of participants, knowledge on HPV-related illnesses and anti-HPV vaccines

| Characteristics of participants | n (%) | Knowledge about HPV and related illnesses (%) |
|--------------------------------|-------|---------------------------------------------|
| Age                            |       |                                             |
| 18-20 y                        | 430 (43) | 184 (43) | 246 (57) |
| >20 y                          | 249 (36.7) | 76 (31) | 173 (69) |
| Gender                         |       |                                             |
| M                              | 225 (33.1) | 104 (46) | 121 (54) |
| F                              | 454 (66.9) | 346 (76) | 108 (24)* |
| Faculty                        |       |                                             |
| Medicine                       | 271 (39.9) | 227 (84) | 44 (16)* |
| Nursing Sciences               | 317 (46.1) | 182 (57) | 135 (43) |
| Humanities (economics, literature) | 23 (3.4) | 2 (9) | 21 (91) |
| Cultural Studies               | 21 (3.1) | 11 (52) | 10 (48) |
| Sciences                       | 47 (6.9) | 6 (13) | (87) |
| Grade                          |       |                                             |
| 1st                            | 220 (32.4) | 86 (39) | 134 (61) |
| 2nd                            | 252 (37.1) | 131 (52) | 121 (48) |
| 3rd                            | 136 (20.0) | 118 (87) | 18 (13)* |
| 4th                            | 71 (10.5) | 41 (58) | 30 (42) |
| Hometown                       |       |                                             |
| Shikoku (Kochi)                | 348 (51) | 123 (35) | 225 (65) |
| Other regions                  | 327 (48) | 137 (42) | 190 (58) |
| Foreign countries              | 4 (1) | 0 (0) | 4 (100) |

Table 1: Characteristics of participants according to knowledge on HPV and HPV-related illnesses. HPV: Human Papillomavirus; n: Number of students; M: Male; F: Female; y: Year; *p<0.05.

The majority of participants were female students, 67%, and most of them were young (18-20 y), 63%; whereas the remaining students were aged 21 years or older. The proportion of participants from nursing faculties was high, 46%, followed by the groups of students from the faculty of medicine (33%), sciences (7%), humanities (3%) and cultural studies (3%). In addition, a greater proportion of participants comprised second 7 graders (37%), followed by first, third and fourth graders (32%, 20%, 11%, respectively). More than half of
participants (53%) was from prefectures other than Kochi, whereas 13% of participants didn’t mention their hometown (Table 1). Characteristics of participants according to knowledge on HPV and HPV-related illnesses Of the participants, 43.2% have already had sexual experience at the time of study, including 36.5% of males and 63.5% of females. In total, 18% of participants had high knowledge on HPV and related conditions (HPV infection/genital warts, genital/anal cancer). Young participants tended to have higher knowledge on HPV and related illnesses as compared with older ones, 43% and 31%, respectively; however, the difference did not reach statistical significance (p>0.05). A greater proportion of female participants, 76%, had high knowledge on HPV and related illnesses (vs. male participants, 46%). When faculty was considered, a high proportion of participants from medical (84%) and nursing (57%) faculties had high knowledge on HPV-related illnesses. In general, medical and nursing students (71%) had high and accurate knowledge on HPV and related illnesses than participants from other faculties (21%) (p<0.05) (Table 1).

On the other hand, third graders (87%) had high knowledge on HPV and related illnesses as compared with fourth (58%), second (52%) and first (39%) graders (p<0.05). No statistically difference was found when comparing groups of participants from different regions of Japan (p>0.05) (Table 1). Overall 59% of the participants knew about HPV vaccines and their importance.

Source of information for HPV vaccines

Results from this study revealed that classmates and friends were the main source of information in regard to HPV vaccines and their indication, 21%. On the other hand, the remaining 79% of participants mentioned other sources of information such as TV, family members, newspapers, sex partner or leaflets from local prefectural government (less than 10% for each source; p<0.05) (not shown).

Rates and determinants of HPV vaccines uptake

![Figure 1: HPV vaccination rate among participants according to gender, age and grade.](image)

This study is limited mainly by its cross-sectional design and the unequal representation of regions or places of permanent residence in the study sample. In addition, the questionnaire used was not a standardized one; it assessed only demographic characteristics, primary prevention, source of information, as no standardized questionnaire was available at the time the survey was conducted (2011-2012). In a future study, the use of the ‘Cervical cancer Knowledge Prevention-64’ [31], and provides more information, is envisaged.

Furthermore, the bivariate analysis showed that ‘having a relative or close person who suffered from cervical cancer was associated with HPV vaccine uptake (O.R.: 2.18; 95% CI: 1.31-3.63; p<0.05); this association remained significant even after adjusting for age and gender (O.R. 2.09; 95% CI: 1.24-3.52; p<0.05) (Table 2).

| Associated Factors                      | Odds ratio | 95% CI       | P-value |
|----------------------------------------|------------|--------------|---------|
| Age (<21 y vs ≥ 21 y)                   | 1.05       | 0.99-1.10    | 0.072   |
| Marital status (Married vs. single)     | 0.42       | 0.12-1.56    | 0.198   |
| Grade (First vs. others)                | 1.33       | 1.33         | 0.212   |
| Faculty (Medical/Nursing vs. others)    | 0.81       | 0.58-1.12    | 0.22    |
| Hometown (Shikoku vs. others)           | 1          | 0.97-1.03    | 0.764   |
| Close person having cervical cancer (Yes vs. No) | 2.18       | 1.31-3.63    | 0.003   |

CI: Confidence Interval; y: Year

Table 2: Determinants of HPV vaccine uptake.

In this study, participants were also asked whether they knew other preventive measures in regard to HPV-related illnesses; 36% of participants supported the ‘condom use’ (8% for abstinence, 2% for medication, and 55% of respondents didn’t know any other preventive measure) (not shown).

Discussion

The present study evaluated the knowledge on HPV, HPV-related conditions, HPV vaccines and to determine the rate of self-reported HPV vaccines uptake in a sample of students from three Japanese universities. Results showed a higher proportion of women having high knowledge on HPV and related illnesses; they were also more aware of the importance of HPV vaccination than their male counterparts.

The overall rate of HPV vaccine uptake was 12% among female participants, which is lower than rates reported by Miyagi and colleagues in a web-based survey conducted in 2010 which included 243 Japanese women (age range: 16-25 years) from Kanagawa prefecture, showing a self-reported HPV vaccination rate of 22% [11]. Another survey conducted among girls in Shiki city, Saitama prefecture (Japan), showed higher rate of HPV vaccination (90.7%) in young girls aged 12-15 years [12] (Table 3).

These high rates may be justified by the fact that officials in those municipalities organized HPV vaccination campaigns for school girls following the adoption of the law on HPV vaccination in the country in 2009 for female teens; in addition, vaccination for this category of population was free of charge. In contrast, a study by Ghotbi and Anai (2012) showed a lower HPV vaccination rate (0.8%) among university students in Beppu city, Kyushu region, Japan [13] (Table 3). This finding is similar to results from a study conducted in Thailand, showing a vaccination rate of 1.2% in a sample of young adult women aged 18-24 years [14].
Lately, several reports showed that HPV vaccination has dramatically decreased in Japan due to extensive anti-HPV vaccination campaigns in the media which suggest the occurrence of adverse effects linked to the vaccines, leading to the suspension of the governmental recommendation for the vaccine [15,16].

| Location           | Age   | Sample size | Vaccination rate (%) | Publication/year |
|--------------------|-------|-------------|-----------------------|------------------|
| Japan/Shiki city   | 12-15 | 1254 (girls)| 90.7                  | Hayashi et al., 2012 |
| Japan/Beppu city   | 17-29 | 245 (woman) | 0.81                  | Ghotbi & Anai, 2012 |
| Japan/Yokohama     | 16-25 | 389 (woman) | 22                    | Miyagi et al., 2014 |
| Japan/Kochi        | 18-27 | 679 (454F; 225M) | 12 (in woman) | Our study |

Table 3: Trend of the rate of HPV vaccine uptake among young Japanese.

This might explain the current trend showing that many young Japanese women are not getting vaccinated, despite being aware of the importance of the vaccines. In Japan HPV vaccination has been included in the National Immunization Program, but in 2013 there were reports on its adverse effects in some girls. This led the government to withdraw its active recommendation of HPV vaccination and definitely suspended it in February 2014 [17].

In our study, when participants were asked about other preventive measures for HPV infection and related complications (cervical cancer, for example), 55% of them didn’t know any other way for prevention, whereas less than half suggested the use of condom. Considering the proportion of participants who were sexually active (43%), a great number of those students may have possibly been exposed to the practice of unsafe sex. Our study also showed that “having a close person who suffered from cervical cancer” was associated with HPV vaccination. This suggests that most of participants might have been affected by the fact of having a sick relative, close friend or the loss of a relative, which motivated them to get vaccinated.

To assure a good coverage of immunization programs, schools and the media play an important role in spreading the information. Our study showed that classmates and friends (21%) were the principal source of information on HPV vaccines, followed by TV (8%), family member (5%); whereas newspapers and sex partner accounted for less than 5% each. This suggests that the media have not been positively supporting the cervical cancer prevention activity in the country. Most anti-HPV vaccination campaigns are led by the media and mostly without scientific proofs, influencing the opinion of the public.

Morbidity and mortality due to cervical cancer are relatively high in countries of the world, including the south-east region of Asia. High morbidity has been reported in India, with 132,000 cervical cancer cases a year, and an incidence and mortality rates of 30.7 per 100,000 and 17.8 per 100,000, respectively [18,19]. Vietnam and Thailand have similar rates (approximately 6,000 cases/year) [20,21]. High incidence has been also reported in Indonesia (15,000 cases/year) and Bangladesh (17,000 cases/year) [18], whereas South Korea (3,888 cases/year), Malaysia (2,000-3,000 cases/year), Singapore (200 cases/year) and Sri Lanka (1,550 cases/year) have lower incidence [22, 23], as shown in Table 4.

| Country    | Incidence (cases/year) | Incidence (per 100,000) | Mortality (per 100,000) | Publication/year |
|------------|------------------------|-------------------------|-------------------------|------------------|
| Japan      | 17,000                 | 6.7-8.0                 | 2.8                     | Konno et al., 2008 [24]; Kim, 2009 [25]. |
| South Korea| 3,888                  | 12.0-15.0               | 3.8                     | Kim, 2009 [25]   |
| Malaysia   | 2,000-3,000            | 10.5                    | 19.7                    | Al-Dubai et al., 2010 [26]; Ezat and Aljunid, 2010 [27]. |
| China      | 5,29,000               | 6.8                     | 3.8                     | Kim, 2009 [25]; Ezat and Aljunid, 2010 [28]; Liu et al., 2013 [30], |
| Taiwan     | -                      | 18.6                    | -                       | Sankaranarayan et al., 2008 [18] |
| India      | 1,32,000               | 30.7                    | 17.8                    | Kaarthigeyan et al., 2012 [19]; Sankaranarayan et al., 2008 [18]. |
| Vietnam    | 6,000                  | -                       | -                       | Castellsagüé et al., 2012 [20] |
| Thailand   | 6,243                  | -                       | -                       | Ferlay et al., 2004 [21] |
| Indonesia  | 15,000                 | -                       | -                       | Castellsagüé et al., 2012 [20] |
| Bangladesh | 13,000                 | 27.6                    | 14.8                    | Ferlay et al., 2004 [21]; Sankaranarayan et al., 2008 [18]. |
| Singapore  | 200                    | 10.6                    | -                       | Tay et al., 2008 [22]; Lee et al., 2011 [23]. |
| Nepal      | 2,150                  | 26.4                    | 14.1                    | Sankaranarayan et al., 2008 [18] |
| Sri Lanka  | 1,550                  | 17.2                    | 9.5                     | Sankaranarayan et al., 2008 [18] |

Table 4: Cervical cancer incidence and mortality in South-East Asian countries.
Considering the incidence and mortality of cervical cancer in Japan (17,000 cases/year; 6.7-8/100,000 and 2.8/100,000 of incidence and mortality rates, respectively) [24,25], there is a need for health policy makers and the government to address the current controversy in regard to the safety of HPV vaccines, searching for scientifically proven evidences. Though the morbidity rate has reached 16,000-28,000 cases a year in the recent 10 years, there are still low rates of cervical cancer screening sessions and HPV vaccination rates being reported in Japan [28,29]. In the South-east region of Asia, China is reported to have one of the highest number of new cases a year (529,000 cases); however, its annual incidence rate is quite similar to that of Japan (6.8/100,000 cases) [30].

This study is limited mainly by its cross-sectional design and the unequal representation of regions of Japan in the study sample. In addition, the questionnaire used in this study was not a standardized one; it assessed only demographics characteristics, primary prevention, source of information, as no standardized questionnaire was available at the time the survey was conducted (2011-2012). In a future study, the use of ‘the Cervical-Cancer-Knowledge-Prevention-64’, which is a validated questionnaire [31], which provides more information, is envisaged.

Nevertheless, the present study is one of the first investigations conducted in Japan that reports on HPV vaccination rate in a relatively big sample of young adults from different places of permanent residence (regions) within the country and with different policies in regard to HPV vaccination. Therefore, results from this study might possibly present the real trend of HPV vaccination rates in Japan. Prevention is better than cure; though cervical cancer screening campaigns currently implemented in the country have to be supported - as they facilitate early diagnosis of HPV related malignancies- health policy makers should likewise do more to promote their prevention.

Conflict of Interest

None declared.

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