Original Article

Human Papilloma Virus [HPV] and Body Mass Index [BMI] in 4,487 Thai Women under Cervical Screening Program

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Objective: To investigate body mass index [BMI] and frequency of human papilloma virus [HPV] infection and determine their association in a Thai woman cohort.

Materials and Methods: Retrospective BMI and HPV genotyping data were retrieved from 4,487 Thai women who participated in a cervical cancer screening program at Chulabhorn Hospital. BMI (kg/m^2) was categorized as less than 18.5 (below normal weight), 18.5 to 22.99 (normal weight), 23.00 to 24.99 (upper range of normal weight), 25.00 to 29.99 (overweight), and greater than or equal to 30.00 (obese), respectively. Linear array HPV testing kit was used to identify 37 HPV types including 12 high-risk [HR], 8 probable high-risk [PR], and 17 low-risk [LR] types.

Results: Of 4,487 participants, 1,078 cases were overweight (24%), 351 cases were obese (7.8%), 801 cases (17.9%) were in the upper range of normal weight, and 1,982 cases (44.2%) were normal. The mean BMI was 23.7 kg/m^2, range 13.8 to 49 kg/m^2, and 15.1%, 6.4%, 3.5%, and 8.4% of the cohort were found to have HPV infection, HR HPV, PR HPV, and LR HPV, respectively. The BMI 25.00 to 29.99 kg/m^2 (overweight) cohort had a statistically significantly lower OR of 0.66 (95% CI 0.47 to 0.93) for HR HPV infection compared with the normal BMI 18.50 to 22.99 kg/m^2 cohort.

Conclusion: About half of the Thai women in this cohort had BMI in the upper range of normal to overweight and obese criteria. Overweight women had a lower rate of HR HPV infection than women with a normal weight.

Keywords: HPV, BMI, overweight, infection, protective factor

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Thailand is a cervical carcinoma endemic area with an age standardized incidence rate of 17.8/100,000 person-year[1]. Obesity and a high body mass index [BMI] are associated with higher risks of many

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diseases, including cervical cancer death[2]. Nutrition and lifestyle factors initiate the development of obesity with the accumulation of excessive adipose tissues, which initiate production of cytokines and other factors in the body to trigger cancer cell growth. Obese individuals are more susceptible to cancer[3]. However, some studies suggest an influence of obesity on human papilloma virus [HPV] infection but further studies are necessary to confirm these results[4].

HPV infection is a causal agent and an essential factor for cervical carcinoma development, found in 99.7% of cases of cervical cancer[5-9]. High risk HPV [HR HPV] infection has been found to be associated with obesity with a lower prevalence of infection observed in obese women[4]. Thus, we aimed to investigate whether BMI is correlated with HPV infection in a large cohort of Thai women.

Materials and Methods

Participants

This study was approved by the Ethical Committee for Human Research of Chulabhorn Research Institute (EC No. 001/2556). HPV genotyping data from 4,550 women aged 20 to 70 years was obtained from July 19, 2011 to November 5, 2012. These data were collected as part of our previously reported study[10]. A total of 63 women were excluded due to absence of a cervix; previous HPV vaccination; history of abnormal cytology, cervical intraepithelial neoplasia [CIN], or cervical cancer; prior HPV infection; diagnosed with any types of active cancer during the last 5 years or unable to follow-up throughout the program.

BMI and weight definition

BMI was calculated as weight in kilograms divided by the square of height in meters and categorized as less than 18.5 (below normal weight), 18.5 to 22.9 (normal weight), 23.1 to 24.9 (upper range of normal weight), 25 to 29.9 (overweight), and greater than or equal to 30 kg/m^2 (obese), respectively, on the basis of standard categories of BMI[11,12].

HPV genotyping

Cervical samples were collected using cytobrushes by gynecologic oncologists or well-trained physicians. The samples were then put in the preservative liquid of the BD SurePath Pap test kit (BD Diagnostics-Tripath, Burlington, NC, USA) for HPV DNA testing[10]. A kit of linear array HPV testing (Roche, USA), capable of identifying 37 HPV types including 12 high-risk [HR], 8 probable high-risk (PR), and 17 low-risk [LR] types classified by oncogenic potentiality, was used[11-14]. In brief, a polymerase chain reaction [PCR] amplified 450 bp fragments from the viral L1 region, then a reverse line blot hybridization system was used to identify 37 HPV genotypes as previously reported[11]. After PCR amplification, the HPV and the β-globin amplicon were hybridized with single LINEAR ARRAY HPV Genotyping Strips coated with HPV and beta-globin probe stripes. If the amplicon consisted of the matching sequence to complementary probe, the biotin-labeled amplicon was hybridized to the oligonucleotide probes. At the probe positions where hybridization occurred, a blue colored complex precipitated. Then, the HPV genotyping strips were visually compared to the HPV genotyping linear array reference guide. The patterns on the strips were compared to the reference for a colorimetric determination of HPV type following the manufacturer's instructions.

Statistical analysis

Descriptive statistical analysis was used to determine distribution types and frequencies of HPV positivity including HR, PR, and LR, along with BMI, sexual intercourse frequencies, and age. Frequency tables were used for qualitative variables. Pearson's chi-square tests were performed to verify the association of demographic data and HPV prevalence. Logistic regression was used to examine odds ratios [OR] and their confidence intervals [CI] of the association between BMI and HPV infection. A $p<0.05$ was defined as statistically significant. Data analysis was performed using Licensed Stata program version 12[10].

Results

Demographic characteristics of the studied population are shown in Table 1. The mean age of the studied population was 44.8 years, range 20 to 70 years, in which 56.4% were married (2,530/4487), 29.4% (1,319/4,487) were single, and 21.8% (976/4,487) were not using contraception. The highest population of the study is normal weight (BMI 18.5 to 22.99 kg/m^2), 44.2%. The mean BMI is 23.7 kg/m^2, range 13.8 to 49.0 kg/m^2. Figure 1 shows that 15.1%, 6.4%, 3.5%, and 8.4% of the cohort were found to have HPV infection, HR HPV, PR HPV, and LR HPV, respectively.

Table 2 shows association of BMI and factors of HPV infection. In the BMI less than 18.5 kg/m^2 group, there was a high rate of HPV infection (51/275, 18.5%),

as compared to 12.8% in the overweight and obese groups. The 20 to 29 years of age group had the highest proportion of HPV positive infection (26.2%) and the divorced group also had the highest proportion of HPV positive infection (19.6%). The current contraception use in life had the highest proportion of HPV positive infection (19.4%) and the frequency of sexual activity group of more than 1 time per week also had the highest HPV infection (21.3%).

The association of BMI and factors of HR HPV infection. In the BMI less than 18.5 kg/m^2 group had the highest proportion of HR HPV positive infection (8.7%). The 20 to 29 years of age group had the highest proportion of HR HPV positive infection (15.2%) and the single and divorced group also had the highest proportion of HR HPV positive infection (8.2%). The current contraception use in life had the highest proportion of HR HPV positive infection, 8.5% and the frequency of sexual activity group of more than 1 time per week also had the highest HR HPV infection, 9.4%. All factors: BMI, age, marital status, contraception use, and frequency of sexual activity had statistically significance in association with HPV and HR HPV infection (Table 2).

Table 3 shows OR (95% CI) of HPV infection according to BMI. The association was found between high BMI and normal rang (Crude OR 0.76 for 25.00 to 29.99 kg/m^2 versus 18.5 to 22.99 kg/m^2 of BMI; p = 0.011) for HPV positivity. Other factors were not found to be significantly associated with HPV infection (adjust OR 0.87 (95% CI 0.70 to 1.09; 0.228).

Table 4 shows OR (95% CI) of HR HPV infection according to body mass index. The cohort in the upper range of normal weight had crude OR 0.68 (95% confidence interval 0.48 to 0.96), p = 0.029, adjusted OR 0.79 (CI = 0.56 to 1.13), p = 0.206, indicating a trend to have a higher rate of HR HPV infection. In addition, the cohort with BMI 25 to 29.99 kg/m^2 (overweight) had a significantly low OR 0.66 (95% CI 0.47 to 0.93), lower than that of the cohort with BMI 18.5 to 22.99 kg/m^2 (normal weight) for HR HPV infection. The cohort with BMI 25 to 29.99 kg/m^2 (overweight) had a significantly low OR of 0.66 (95% CI 0.60 to 0.91) for HR HPV positivity. The cohort with BMI ≥30 kg/m^2 (obese) was not found to be significantly associated with HPV infection (HPV negative, HPV positive, HR HPV, and LR HPV) other than for PR HPV, OR 0.23 (95% CI 0.07 to 0.72).

Discussion

There was a study which found the risk of HR-HPV infection was significantly lower among those who were overweight (OR = 0.817, 95% CI 0.680 to 0.982), or obese (OR = 0.688, 95% CI 0.556 to 0.851) when compared with normal weight women[4]. Our study found the HR HPV infection rate was significantly lower among overweight women, adjusted OR 0.66 (95% CI 0.47 to 0.93). However, in obese women, there was no statistically significant difference.

A higher rate of infection in obese women when compared with normal weight women can be caused by alterations of adipokines, for example adiponectin, leptin, IL-6, and TNF-α. Leptin might be a key factor because of its strong pro-inflammatory qualities such as activation of T lymphocytes and neutrophils, and secretion control of macrophages, monocytes, and cytokines[15,16]. Leptin deficiency increases susceptibility to infection in animal models[17,18]. However, a previous clinical report found that BMI was correlated with leptin increases, which

Table 1. Demographic characteristics of the studied population

Demographics	Total, n (%)
n	4,487
Age (years)	
Mean ± SD	44.8±10.8
Range	20 to 70
20 to 29 years	409 (9.1)
30 to 39 years	1,063 (23.7)
40 to 49 years	1,443 (32.2)
≥50 years	1,572 (35.0)
Marital status	
Single	1,319 (29.4)
Married	2,530 (56.4)
Divorced	638 (14.2)
Contraception use	
Never	976 (21.8)
Ever	1,482 (33.0)
Current	2,029 (45.2)
Frequency of sexual activity	
No	1,614 (36.0)
Least than 1 times per month	572 (12.7)
1 to 4 times per month	1,728 (38.5)
>1 times per week	573 (12.8)
BMI (kg/m^2)	
Mean ± SD	23.7±4.1
Range	13.8 to 49
<18.5	275 (6.1)
18.5 to 22.99	1,982 (44.2)
23.00 to 24.99	801 (17.9)
25.00 to 29.99	1,078 (24.0)
≥30.00	351 (7.8)

Table 2. Association of BMI and other factors with HPV infection

Demographics	HPV		*p*-value	HR HPV		*p*-value
	Negative (n = 3,795)	Positive (n = 692)		Positive (n = 292)	Negative (n = 4,195)	
BMI			0.017*			0.002*
<18.5	224 (81.5)	51 (18.5)		251 (91.3)	24 (8.7)	
18.5 to 22.99	1,660 (83.8)	322 (16.2)		1,826 (92.1)	156 (7.9)	
23.00 to 24.99	665 (83.0)	136 (17.0)		757 (94.5)	44 (5.5)	
25.00 to 29.99	940 (87.2)	138 (12.8)		1,030 (95.5)	48 (4.5)	
≥30.00	306 (87.2)	45 (12.8)		331 (94.3)	20 (5.7)	
Age			<0.001*			<0.001*
20 to 29 years	302 (73.8)	107 (26.2)		347 (84.8)	62 (15.2)	
30 to 39 years	862 (81.1)	201 (18.9)		972 (91.4)	91 (8.6)	
40 to 49 years	1,233 (85.4)	210 (14.6)		1,361 (94.3)	82 (5.7)	
≥50 years	1,398 (88.9)	174 (11.1)		1,515 (96.4)	57 (3.6)	<0.001*
Marital status			<0.001*			
Single	1,080 (81.9)	239 (18.1)		1,211 (91.8)	108 (8.2)	
Married	2,202 (87.0)	328 (13.0)		2,398 (94.8)	132 (5.2)	
Divorced	513 (80.4)	125 (19.6)		586 (91.8)	52 (8.2)	
Contraception use			<0.001*			<0.001*
Never	902 (92.4)	74 (7.6)		944 (96.7)	32 (3.3)	
Ever	1,258 (84.9)	224 (15.1)		1,394 (94.1)	88 (5.9)	
Current	1,635 (80.6)	394 (19.4)		1,857 (91.5)	172 (8.5)	
Frequency of sexual activity			<0.001*			<0.001*
No	1,440 (89.2)	174 (10.8)		1,554 (96.3)	60 (3.7)	
Least than 1 times per month	483 (84.4)	89 (15.6)		533 (93.2)	39 (6.8)	
1 to 4 times per month	1,421 (82.2)	307 (17.8)		1,589 (92.0)	139 (8.0)	
>1 times per week	451 (78.7)	122 (21.3)		519 (90.6)	54 (9.4)	

Data are presented as n (%), * $p<0.05$
HPV = human papillomavirus; HR HPV = high risk human papillomavirus

Table 3. OR (95% CI) of HPV infection according to BMI

Demographics	Crude OR (95% CI)	*p*-value	Adjusted OR (95% CI)	*p*-value
BMI				
<18.5	1.17 (0.85 to 1.63)	0.336	0.98 (0.70 to 1.38)	0.906
18.50 to 22.99	1	-	1	-
23.00 to 24.99	1.05 (0.85 to 1.31)	0.637	1.20 (0.95 to 1.51)	0.118
25.00 to 29.99	0.76 (0.61 to 0.94)	0.011*	0.87 (0.70 to 1.09)	0.228
≥30.00	0.76 (0.54 to 1.06)	0.105	0.89 (0.63 to 1.26)	0.525

Adjusted = age, marital status, contraception use, frequency of sexual activity; OR = Odds ratio
* $p<0.05$

suggests that obese patients with leptin resistance may have a susceptibility to infection[19,20]. These may be a result of obesity group in our study had a higher infection rate of HR HPV infection compared to the overweight group (5.7 vs. 4.5%). In addition, there are other explanations that can be discussed such as obese women may change sexual behaviors associated with deterioration in every step of sexual function, including arousal, lubrication, satisfaction, orgasm, and sexual desire[21-23]. Another study reported that thinner people

Table 4. OR (95% CI) of HR HPV infection according to BMI

Demographics	Crude OR (95% CI)	*p*-value	Adjusted OR (95% CI)	*p*-value
BMI				
<18.5	1.12 (0.71 to 1.75)	0.623	0.86 (0.54 to 1.37)	0.517
18.50 to 22.99	1	-	1	-
23.00 to 24.99	0.68 (0.48 to 0.96)	0.029*	0.79 (0.56 to 1.13)	0.206
25.00 to 29.99	0.54 (0.39 to 0.76)	<0.001*	0.66 (0.47 to 0.93)	0.019*
≥30.00	0.71 (0.44 to 1.14)	0.157	0.88 (0.54 to 1.44)	0.623

Adjusted = age, marital status, contraception use, frequency of sexual activity; OR = Odds ratio
* $p<0.05$

of both genders were generally more sexually-attractive, and in healthy women aged 19 to 40 years, frequency of penile-vaginal intercourse had inverse variation with the hip size in which implied to be as BMI[24]. Thus, for these reasons, women who have a high BMI seem to have a lower sexual activity. Because the most important primary risk factor for HPV infection is sexual intercourse, it can be implied that the risk for HR-HPV infection is lower in high-BMI women because of decreased sexual intercourse. In our study, obesity group does not have statistically significant higher risk of HPV infection because of low sexual activity despite leptin resistance and a high suscepibility to infection. Although in our study, overweight women (BMI 25.00 to 29.99 kg/m^2) had a lower rate of HR HPV infection than other BMI groups, this could be because overweight women had the second lowest rate (62.52%) of current sexual intercourse, which might cause a lower rate of cervical HPV infection. In addition, the obese patients had the lowest frequency of sexual intercourse, 53.6%. In obese women, the PR HPV infection rate was low (OR 0.23, 95% CI 0.07 to 0.72). Thus, a higher BMI has a trend to be a protective factor against cervical HPV infection, especially in overweight women. Hence, the overweight group has the lowest rate of HR HPV infection. Moreover, it is possible that as the women get older, the more weight they gains and the lesser HPV infection is found due to decreasing quantity of sexual intercourse. This should have multivariate analysis to confirm in the future.

Strength of our study is a large sample size of Thai population. However, a limitation of our study is the low rate of HPV infection study group therefore, additional studies should be performed to confirm our results.

Conclusion

Overweight women (BMI 25.00 to 29.99 kg/m^2) had a lower rate of HR HPV infection than women with a normal weight. Higher BMI might have a tendency to be a protective factor against HPV infection.

What is already known on this topic?

Higher BMI might have a tendency to be a protective factor against HPV infection, especially in overweight women.

What this study adds?

Higher BMI might have a tendency to be a protective factor against HPV infection, especially in overweight women.

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Potential conflicts of interest

The authors declare no conflict of interest.

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