

## RESEARCH ARTICLE

# Relationship Between the Body Mass Index and Abnormal Pap Smears

Russameekae Prompakay<sup>1</sup>, Supanee Promthet<sup>1\*</sup>, Siriporn Kamsa-ard<sup>2</sup>, Krittika Suwanrungruang<sup>3</sup>, Surapon Wiangnon<sup>4</sup>, Peter Bradshaw<sup>1</sup>

### Abstract

This cross-sectional analytic study aimed to investigate any relationship between the body mass index (BMI) and an abnormal Pap smear. The subjects were 7,720 women aged 30-69 years who lived in Khon Kaen Province, Thailand, and had been recruited as participants in the Khon Kaen Cohort Study during 1990-2001. All had received Pap smear screening for cervical cancer. The data were analyzed using descriptive and inferential statistics. Multiple logistic regression was used to determine the relationship between body mass index and an abnormal Pap smear. The mean BMI was 24.53kg/m<sup>2</sup> (SD=3.98), and 2.14% had abnormal Pap smears. Compared with the reference group of women with a BMI  $\leq$ 22.9kg/m<sup>2</sup>, those with a body mass index of 23.0-24.9kg/m<sup>2</sup> had a reduced risk of an abnormal smear (OR<sub>adj</sub>=0.92, 95% CI: 0.57-1.47), but women with a BMI 25.0-29.9kg/m<sup>2</sup> were found to have an approximately 1.24 times higher risk (OR<sub>adj</sub>=1.24, 95% CI: 0.86-1.80), and those with a BMI  $\geq$ 30.0kg/m<sup>2</sup> had an approximately 1.63 times higher risk (OR<sub>adj</sub>=1.63, 95% CI: 0.98-2.69). The results indicated that the risk of Pap smear abnormalities is increased in women who have a higher than normal body mass index, but this finding was not statistically significant. Nevertheless, public health personnel should encourage women to maintain their BMI in the normal range to reduce the possible future risk of cervical cancer.

**Keywords:** Body mass index - Pap smear - Thailand

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### Introduction

Cervical cancer is the third most common cancer in women worldwide and the second most common for women in developing countries. Globally, it ranks as the fourth leading cause of death in women. In 2008, there were 529,800 new cervical cancer cases (age-standardized incidence rate: 15.2 per 100,000 women) and 275,100 deaths from cervical cancer (age-standardized mortality rate: 7.8 per 100,000 women). Most cervical cancer cases and deaths (more than 85%) are in developing countries, and 159,800 deaths were in Asia (Ferlay et al., 2010a; Jemal et al., 2011).

In Thailand, cervical cancer is the second most common cancer in females after breast cancer, and it ranks as the second biggest cause of death after liver cancer (Khuhaprema et al., 2012a). In 2008, there were 9,999 new cervical cancer cases (age-standardized incidence rate: 24.5 per 100,000 women) and 5,216 deaths from cervical cancer (age-standardized mortality rate: 12.8 per 100,000 women). It is estimated that in 2015, there will be 13,082 new cervical cancer cases (Ferlay et al., 2010b).

Pap smear is the common technique for cervical cancer screening. If the patients are detected at early stage, this

is expected reduce the subsequent burden of cervical cancer, and a recent systematic review and meta-analysis has confirmed that cervical screening appears to provide protective benefits in terms of its association with a reduction in the incidence of invasive cervical cancer and the subsequent mortality rate (Peirson et al., 2013).

For women with an abnormal Pap smear, the chances of having invasive cervical carcinoma vary according to type of abnormal cells detected: approximately 0.1-0.2% of women with atypical squamous cells (ASC), less than 1-9% of women with atypical glandular cells (AGC), and 1-2% of women with high-grade squamous intraepithelial lesion (HSIL) (Wright et al., 2002). In Thailand, positive Pap smears are found in about 1.5% of women attending a cervical cancer screening programme (Khuhaprema et al., 2012b).

Obesity or overweight is a risk factor for many chronic diseases, including cancer (Calle et al., 2003; Renehan et al., 2008). There are numerous studies which show that body mass index (BMI) has an association with the incidence of various cancers in women such as cancers of the breast, endometrium, esophagus and gall bladder (Renehan et al., 2008), and the liver (Jee et al., 2008). There are also studies which have found a positive association

<sup>1</sup>Department of Epidemiology, <sup>2</sup>Department of Biostatistics and Demography, Faculty of Public Health, <sup>3</sup>Cancer Unit, <sup>4</sup>Department of Pediatrics, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand \*For correspondence: [supanee@kku.ac.th](mailto:supanee@kku.ac.th)

with the incidence of cervical cancer (Parazzini et al., 1988; Wolk et al., 2001; Lacey et al., 2003; Appleby et al., 2007; Lee et al., 2013). A range of factors have been found to be associated with abnormal Pap smears: these include human papilloma virus (HPV) infection (Rositch et al., 2013), smoking (Ward et al., 2011), sexually transmitted infections (apart from HPV), young age at first sexual intercourse, multiple sexual partners, and high parity (Kruger-Kjaer et al., 1998, Claeys et al., 2002). However, data on a possible association between high BMI and a positive pap smear are scarce, and only one relevant study was found. In a study of postmenopausal women in South Korea, abnormal smears were more frequently found in those with higher BMIs (Ahn et al., 2012).

We therefore conducted this study to investigate the relationship between BMI and an abnormal Pap smear in Thai women.

### Materials and Methods

This cross-sectional analytic study was conducted during 2012-2013 in Khon Kaen, Thailand. The subjects were 7,720 women aged 30-69 years living in Khon Kaen Province who had been recruited in 1990-2001 for the Khon Kaen Cohort Study (Sriamporn et al., 2005) and had all received Pap smear screening for cervical cancer. Information about BMI at recruitment and other variables of interest such as age, education, income, age at first sexual intercourse, parity, number of sexual partners, history of sexually transmitted infection, oral contraceptive use and smoking was available in the Khon Kaen cohort study database. The data were analyzed using descriptive and inferential statistics. In a univariate analysis, crude odds ratios (OR) and p values were calculated to investigate the associations between variables of interest and an abnormal Pap smear. Those variables with a p value  $\leq 0.25$  were entered into a multiple logistic regression analysis using backward elimination to adjust for confounding factors.

#### Ethical approval

The research study was approved according to the 1975 Declaration of Helsinki by the Khon Kaen University Ethics Committee for Human Research (Reference No. HE551381, dated 27 November 2012).

### Results

Table 1 summarises the characteristics of all 7,720 women included in the study. The vast majority (94.2%) had not received education beyond primary school level, and most (84.3%) reported an average family income of less than 5000 Baht per month. Their mean BMI was 24.5kg/m<sup>2</sup>, and 165 were recorded as having an abnormal Pap smear. Table 2 shows the results of the univariate analysis. While no statistically significant relationship was found between BMI and an abnormal Pap smear, the risk of an abnormal Pap smear grew larger as BMI levels increased.

The multivariate analysis showed a similar non-significant trend. When compared to women with a BMI

**Table 1. Characteristics of Participants in the Study (n=7,720)**

| Characteristics   | Total | %    |
|---|-------|------|
| Pap result  |       |      |
| Negative  | 7,555 | 97.9 |
| Positive  | 165   | 2.1  |
| Body mass index (kg/m <sup>2</sup> )                            |       |      |
| $\leq 22.9$   | 2,850 | 36.9 |
| 23.0-24.9   | 1,499 | 19.4 |
| 25.0-29.9   | 2,655 | 34.4 |
| $\geq 30.0$   | 716   | 9.3  |
| Mean (SD)=24.5 (4.0), Median (Min:Max)=24.3 (14.9:39.8)         |       |      |
| Age (year)  |       |      |
| $\leq 39$   | 776   | 10   |
| 40-44   | 902   | 11.7 |
| 45-49   | 1,787 | 23.1 |
| 50-54   | 1,706 | 22.1 |
| 55-59   | 1,309 | 17   |
| $\geq 60$   | 1,240 | 16.1 |
| Mean (SD)=50.6 (8.1), Median (Min:Max)=51 (30:69)               |       |      |
| Education completed   |       |      |
| Primary school  | 7,275 | 94.2 |
| High school   | 445   | 5.8  |
| Average income of the family (bath/month)                       |       |      |
| <5,000  | 6,507 | 84.3 |
| $\geq 5,000$  | 1,213 | 15.7 |
| Mean (SD)=3,126.9 (5,821.8), Median (Min:Max)=2,000 (0:200,000) |       |      |
| Parity  |       |      |
| $\leq 1$  | 599   | 7.8  |
| >1  | 7,121 | 92.2 |
| Median (Min:Max)=3 (0.0:19.0)                                   |       |      |
| Age at first sexual intercourse (year)                          |       |      |
| $\geq 18$   | 6,025 | 78   |
| <18   | 1,695 | 22   |
| Mean (SD)=19.9 (4.6), Median (Min:Max)=20 (9.0:55.0)            |       |      |
| Number of sexual partners                                       |       |      |
| 1   | 6,879 | 89.1 |
| $\geq 2$  | 841   | 10.9 |
| Median (Min:Max)=1 (1.0:10.0)                                   |       |      |
| Oral contraceptive use (n=6,602)                                |       |      |
| No  | 4,216 | 63.9 |
| Yes   | 2,386 | 36.1 |
| Cigarette smoking (n=7,407)                                     |       |      |
| No  | 7,362 | 99.4 |
| Yes   | 45    | 0.6  |
| STI history (n=6,739)   |       |      |
| No  | 5,500 | 81.6 |
| Yes   | 1,239 | 18.4 |

\*STI=sexually transmitted infection

**Table 2. Factors Association with Abnormal Pap smear (n=7,720)**

| Variables                                 | Total | Abnormal Pap smear | Crude OR | 95% CI    | p value |
|---|-------|--------------------|----------|-----------|---------|
| Body mass index (kg/m <sup>2</sup> )      |       |                    |          |           |         |
| $\leq 22.9$                               | 2,850 | 54                 | 1        | -         | 0.145   |
| 23-24.9                                   | 1,499 | 26                 | 0.91     | 0.57-1.47 |         |
| 25-29.9                                   | 2,655 | 63                 | 1.26     | 0.87-1.82 |         |
| $\geq 30.0$                               | 716   | 22                 | 1.64     | 0.99-2.71 |         |
| Age (year)                                |       |                    |          |           |         |
| $\leq 39$                                 | 776   | 19                 | 1        | -         | 0.476   |
| 40-44                                     | 902   | 21                 | 0.95     | 0.51-1.78 |         |
| 45-49                                     | 1,787 | 46                 | 1.05     | 0.61-1.81 |         |
| 50-54                                     | 1,706 | 35                 | 0.83     | 0.47-1.47 |         |
| 55-59                                     | 1,309 | 21                 | 0.65     | 0.35-1.22 |         |
| $\geq 60$                                 | 1,240 | 23                 | 0.75     | 0.41-1.39 |         |
| Education (school)                        |       |                    |          |           |         |
| Primary                                   | 7,275 | 156                | 1        | -         | 0.862   |
| High                                      | 445   | 9                  | 0.94     | 0.48-1.86 |         |
| Average income of the family (bath/month) |       |                    |          |           |         |
| <5,000                                    | 6,507 | 146                | 1        | -         | 0.119   |
| $\geq 5,000$                              | 1,213 | 19                 | 0.69     | 0.43-1.12 |         |
| Parity                                    |       |                    |          |           |         |
| $\leq 1$                                  | 599   | 8                  | 1        | -         | 0.132   |
| >1  | 7,121 | 157                | 1.67     | 0.81-3.41 |         |
| Age at first sexual intercourse (year)    |       |                    |          |           |         |
| $\geq 18$                                 | 6,025 | 121                | 1        | -         | 0.149   |
| <18                                       | 1,695 | 44                 | 1.3      | 0.92-1.84 |         |
| No. of sexual partners                    |       |                    |          |           |         |
| 1   | 6,879 | 147                | 1        | -         | 0.995   |
| $\geq 2$                                  | 841   | 18                 | 1        | 0.61-1.64 |         |
| Oral contraceptive use                    |       |                    |          |           |         |
| No  | 4,216 | 82                 | 1        | -         | 0.82    |
| Yes                                       | 2,386 | 59                 | 1.01     | 0.96-1.06 |         |
| Cigarette smoking                         |       |                    |          |           |         |
| No  | 7,362 | 160                | 1        | -         | 0.04    |
| Yes                                       | 45    | 3                  | 0.88     | 0.76-1.02 |         |
| STI history                               |       |                    |          |           |         |
| No  | 5,500 | 116                | 1        | -         | 0.048   |
| Yes                                       | 1,239 | 37                 | 0.94     | 0.88-1.00 |         |

\*STI=sexually transmitted infection; OR=Odds Ratio

$\leq 22.9 \text{ kg/m}^2$  (reference group), women with a BMI 23.0-24.9  $\text{kg/m}^2$  had an about 8% decreased risk of abnormal Pap smear (95%CI: 0.57-1.47), while women with BMI 25.0-29.9  $\text{kg/m}^2$  had an approximately 1.24 times higher risk of abnormal Pap smear (95%CI: 0.86-1.80) and those with a BMI  $\geq 30.0 \text{ kg/m}^2$  had an approximately 1.63 times higher risk of abnormal Pap smear (95%CI: 0.98-2.69).

## Discussion

While this study failed to find any the statistically significant relationship between BMI and an abnormal Pap smear, the results nevertheless indicated that the higher the BMI, the greater were the risks of an abnormal Pap smear.

One obvious explanation for this non-significant, but apparent association, is that overweight/obesity may lead to an increased risk of cervical cancer, and one possible mechanism for this is that obesity can cause increased serum sex hormone levels which have been linked to a higher risk of cancers of the female reproductive tract (Siiteri, 1987; Lacey et al., 2003).

However, there is a different kind of explanation which is independent of any connection between obesity and a higher incidence of cervical cancer, and this relates to the findings which indicate that obese women are less likely to undergo cervical cancer screening. In a German study (Meisinger et al., 2004) obese women aged 50 years and older were less likely to obtain cancer screening (including Pap smears) than women of normal weight. In a systematic review and meta-analysis of studies conducted in the USA to investigate whether BMI is related to attendance for Pap smear screening (Maruthur et al., 2009), 10 of the 11 relevant studies identified indicated an inverse association between BMI and attendance. National and cultural differences may well mean that this finding cannot be generalised to Thai women, but, to the extent that it can, then it may mean that obese women in Northeast Thailand tend to obtain cervical screening only after symptoms or clinical signs of cervical cancer develop or at an age when the risk of cervical cancer becomes recognised as a real possibility. These are issues which cannot be answered by the present study and can only be resolved by future research.

With regard to the reason why the result failed to reach statistical significance, one possibility has to do with the age composition of the subjects in the present study and the time-lapses between the onset of obesity and the Pap smear. For example, if obesity does eventually lead to the development of cervical cancer, given the cross-sectional nature of the present study, then for many women the time between onset of obesity and a subsequent development of abnormal cervical cells may have been too short for the finding of an abnormal Pap smear. This certainly suggests a limitation of the present study and the need for future prospective studies.

In spite of its limitations, to the best of our knowledge, this is only the second study to investigate an association between BMI and Paps smear abnormalities. As such, it raises a number of important issues for future research to clarify the nature of a possible association.

In conclusion, the findings of this study showed that

the risk of Pap smear abnormalities is increased in women who have a higher than normal BMI, but this increased risk was not statistically significant. This finding is discussed with respect to possible explanations and the need for future research, especially in a Thai population. Nevertheless, public health personnel should continue encourage women to maintain their BMI in the normal range because this may well reduce the risk of cervical cancer in the future.

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