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Adequacy of Papanicolaou Cytologic Smear and Factors Related to Abnormal Findings

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ABSTRACT

Objective: To evaluate the adequacy of the Papanicolaou (Pap) cytologic smear taken in Pasir Mas Health Clinic and to determine the factors associated with abnormal Pap smear.
Design: A cross sectional study from January to December 2004.
Methods: All 290 'Pap Smear Request and Report Form' in that year were evaluated. The health personnel who did the procedure filled the form and the pathologist gave results. The form consisted of four main sections- hospital/clinic description, demographic data, clinical summary and laboratory results. All information in the forms was analyzed.
Results: Out of 290 forms, 238 (82.1%) were complete and included in the study. The adequacy of specimen that was categorized as 'satisfactory' was 135(56.7%), 'satisfactory for evaluation but limited by' was 95(40.0%) and 'unsatisfactory' 8(3.3%). Fifty-four (22.7%) showed abnormal results in which 52(96.3%) of them had benign cellular changes and 2(3.7%) had epithelial cells abnormalities. In multiple logistic regression analysis, satisfactory adequacy of specimen (OR=3.26, 95%CI: 1.59, 6.68) and having symptoms of discharge or abnormal bleeding (OR=9.14, 95%CI: 1.62, 51.47) were associated with abnormal Pap smear results.
Conclusions: Percentage of unsatisfactory specimen taken for Pap smear screening is relatively high. Therefore further evaluation, education and training need to be given to health personnel involved, as it is one of the important associated factors for abnormal results.

Keywords: Papanicolaou smear, cervix neoplasms, smear adequacy

INTRODUCTION

Ministry of Health in Malaysia introduced Papanicolaou (Pap) smear screening program since 30 years ago. The target population was women aged 20 to 65 year aimed for early detection of cervical cancer. Despite its rapid, non-invasive and painless procedure, it remained underused by some women. A study by Chee et al. (1) in 2003 found only 6.4% of electronics women worker had done the procedure at least once. National Health Morbidity Survey II (2) approximated that 30% of 10.5 million women in Malaysia were in the reproductive age or older. As cervical cancer is the second most common cancer among females in Malaysia, with the high number of women in reproductive age, it is very important to practice Pap smear for screening.

In order the Pap smear screening to be effective in detection of precursor lesion, wide coverage of the target group population, quality of smear collection and the management of abnormal cytology were the important factors. The sampling of smears depends on the technique and skill of the operator, and the sampling devices used. These factors affect the

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coverage of sampling of the whole transformation zone. Sufficient specimens need to be ensured to allow detection of abnormal findings. Poorly taken smears might contribute to false-negative results (3, 4). An unsatisfactory report necessitates patient retesting, the result of which is added health care cost and patient inconvenience. Therefore, the aims of this study were to evaluate the adequacy of the Pap smear specimen taken in Pasir Mas Health Clinic and to determine the factors associated with abnormal Pap smear results.

METHODS

A cross sectional study was carried out at Pasir Mas Health Clinic. It is the public health clinic that offers maternal and child health care in Pasir Mas district, one of ten districts in Kelantan. We reviewed all 'Pap Smear Request and Report Form' from 1st January to 31st December 2004. The form was used in all health centers and hospitals in Kelantan. It has four parts, which were the patient's demographic data, hospital or clinic description, clinical summary and laboratory reports. The first, second and third parts were completed by the health personnel who did the Pap smear procedure, while the fourth part by the pathologist in Kota Bharu Hospital who reviewed the specimen.

The information included in the clinical summary are last menstrual period, method of contraception, hormonal status, symptoms and signs, indication for Pap smear and date of last Pap smear. The fourth part included reports on adequacy of the specimen, general categorization and descriptive diagnosis. The report was based on the Bethesda System Criteria 1991 that were satisfactory for evaluation, 'satisfactory but limited by' and unsatisfactory for evaluation. For 'satisfactory but limited by' cases, the cytology report noted whether it was limited by inadequate squamous epithelial cells, lack of endocervical cells transformation zone component, poor fixation, air drying artifact, blood thick smear, thick inflammatory exudates or lack of clinical data. Reasons for unsatisfactory report include broken slaid, scanty squamous epithelial component, obscuring blood, inflammation, thick areas or poor fixation and air drying artifact. General categorization and descriptive diagnosis were reported as within normal limits, benign cellular changes (BCC) due to reactive changes or infection, and epithelia cells abnormalities that were squamous cells and glandular cells abnormalities. All forms, total of 290, were included and reviewed in this study. Permission was taken from Pasir Mas Medical Officer of Health. All of the smears were taken as screening and method used to analyse the smear was conventional method.

Statistical analysis

Age, parity and age at marriage were presented as mean and standard deviation (SD) as they were normally distributed. The mean age, parity and age of marriage between normal and abnormal Pap smear results group were compared by independent t test. The categorical variables were expressed as frequency and percentage. Chi square test or Fisher's Exact test was used accordingly to determine the associated factors for abnormal results in univariate analysis. Level of significance was set at 0.05.

Multiple Logistic Regression was applied to determine the associated factors for abnormal result, as the variable under interest was binary in nature. All variables were included in the multivariate analysis. Backward and forward stepwise logistic regression was used. The final model was obtained by using likelihood ratio test based on maximum likelihood estimates. The fit of the final model was checked by applying Hosmer Lemeshow test, overall classification of correct outcome and area under the receiver operating characteristic (ROC) curve. The multivariate analysis results were presented with adjusted odds ratio (OR), and its 95% confidence interval (95%CI) and P values. Data entry and data analysis were done using Statistical Package for Social Science (SPSS) Version 12.0.

RESULTS

Fifty-two (17.9%) forms were excluded from the study due to its incompleteness. The mean age was 34.9 (SD 8.1) year and mean parity was 4.1(SD 2.4) with range of 1 to 12 children. The mean age at marriage was 22.4(SD 4.4), ranged from 15 to 41 years. Two hundred and thirty four (98.3%) was Malays and others were Siamese. The descriptive results of clinical summary and Pap smear findings were presented in table 1.

Majority of the women did the Pap smear at perimenopausal (92.0%) and without any symptom at the presentation (97.1%). Common methods used to acquire sample were using cervical scrape or combination of scrape with endocervical brush. Only 136(56.7%) of the sample taken were satisfactory and 8(3.3%) were unsatisfactory, others were 'satisfactory but limited by'.

Most of the findings were within normal limit, 183(77.0%). BCC due to reactive changes was mainly due to inflammation and also atrophy with inflammation. The causes for BCC due to infection were coccobacillis, Candida spp and Actinomycess spp. The squamous cell abnormality found in one woman was due to Human Papiloma Virus (HPV) while the glandular cells change was atypical glandular cells

of undetermined significance (AGUS).

To determine the associated factors for abnormal result, the 'satisfactory but limited by' group was grouped together with unsatisfactory for evaluation, as unsatisfactory result group, total of 103 samples. Univariate analysis showed that the mean age, age at marriage and parity was not significantly difference between the normal and abnormal results. However, adequacy of specimen, present of symptoms at presentation and method of contraception were the significant associated factors (table 2).

The final model for associated factors for abnormal result by multiple logistic regression was shown in table 3. The significance factors were satisfactory smear with OR=3.26 (95%CI: 1.59, 6.68) and present of symptom, OR=9.14 (95%CI: 1.62, 51.47) when adjusted for age, parity, age at marriage, condition of cervix and contraceptive used.

DISCUSSION

The percentage of satisfactory and unsatisfactory smear in this study was 56.7% and 3.3% respectively, comparable to the study by Migliore et al. (5). He reported that the satisfactory smear ranged from 60% to 70% and unsatisfactory smear was 1.7% to 4.2%. A range of 2.6% to 6.8% of inadequate cervical cytology has been reported by Wilson et al. (6). Sixteen point five percent (16.5%) of cervical smear were classified as 'satisfactory but limited by' or unsatisfactory (7). The method used in smearing process was the conventional method, which has been reported to have many limitations that include a significant false negative and false positive rate, also a significant unsatisfactory rate (8, 9). Despite adequate care in preparing the conventional smear, only about 20% of cells are effectively transferred to the slide (8).

Bar-Am et al. (7) divided the causes of unsatisfactory smear into two main groups, technical factors and sampling errors. He reported that only 1% of unsatisfactory smear was due to technical factors that occurred during smear preparation resulting in poor dispersion of cells. However, sampling errors that occurred during sampling collection (missed of transformation zone, excessive exudates and excessive pressure) contributed 15.1% to unsatisfactory smear. In our study, 'satisfactory but limited by' smear was also mainly due to lack of endocervical cells transformation zone. This is important because dyskaryosis was more likely to be detected in smears that contained endocervical cells than in those without such cells (4,10). Atypia was detected more frequently in samples with endocervical cells (11).

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An effective smear was also related to the types of devices used to collect specimen. Meta-analysis studies by Bauman (12) and Williamson et al. (4) found that there was a significant increased in endocervical cells when the cervical brush was used alone or combination with spatula compared to a spatula alone. Types of spatula itself determined the adequacy of endocervical cells collection. Extended-tip spatulas of various designs were better than the Ayre design. Cytobrush with an extended tips spatula was the best combination (10). In Pasir Mas Health Clinic, 49% of the health personnel used scrape or spatula alone to take the specimen. Despite the other 49% practiced both spatula and endocervical brush, it still depended on the technique used, as Eisenberger et al. (13) has reported that the quality of a smear could be improved by using the spatula first followed by endocervical brush, as the brush could provoke bleeding from columnar epithelium, which resulted in contaminated smear.

Besides modification of the smear-taking devices to improve methods of collection and preparation, taking more than one smear was also suggested. Preparing one additional smear per cervical scrape increased the rate of detection of abnormal cells (14). Bentz et al. (15) also proved that reprocessing of unsatisfactory thin prep samples reduced the overall unsatisfactory rate and improved detection of cellular abnormalities. Human factors were the main contributors to the smear's adequacy. The ability to obtain adequate sampling improved with experience and correlated directly with total number of smears taken annually (7). The performance of the person who took the smear was an important component of Pap smear screening practice (11). To produce a cervical sample with adequate squamous columnar cells, skills in patient preparation, specimen collection, laboratory processing and slide interpretation were required (16).

Adequacy of specimen is an important associated factor for abnormal Pap smear result in this study. The risk of detection an abnormal result was three times higher when the specimen taken was satisfactory. Therefore, a good and adequate specimen is important to improve detection of abnormal cells. Further steps to improve the adequacy of specimen need to be taken seriously. The American Society for Colposcopy and Cervical Pathology recommended that Pap test result should be repeated within a short interval of two to four months in women with unsatisfactory result (17). This could prevent misdetection of abnormal cells. If the women came with symptom at presentation, either abnormal bleeding or discharge, the risk of having abnormal Pap smear result was about nine times compared to those asymptomatic. This is supported by a study by Pretorius et al. (18) that 56% of patients with cervical cancer presented with abnormal vaginal bleeding. However, in our study, there was a small sample size of women with symptom, which resulted to a wide confidence interval.

Based on the findings of this study, improvements in patient preparation, technique and health personnel skills are needed. Regular monitoring of techniques by the health personnel is important to detect the incompetence staffs in performing Pap smear. This group of staffs needs to be trained to improve their skills in obtaining satisfactory specimen. Training all staffs involved is also important to update their knowledge on current technique. Further study with larger sample size with inclusion of the health personnel information is suggested. The other simple technique suggested by Kotaska and Matisic (19) in their study, was appropriate cervical cleaning. The study has shown that routine cervical cleaning with an oversized cotton swab before obtaining Pap smear could improve its quality and enhancing the efficiency and effectiveness of cervical cancer screening. Appropriate cleaning reduced the frequency of smears with inflammatory exudates or inadequate endocervical cells, and increased frequency of smears with inadequate cellularity. To ensure optimal quality of Pap smear reading, a quality assurance program for laboratories needs to be instituted. Current practice is that only 10% of the negative smears are re-screened but it is hoped that in the future, all of them will be re-screened.

It is also recommended that more advanced cytology technique will be used, such as liquid-based technology. It is based on the suspension of cells in preservative fluid rather than smearing on a glass slide. This results in distribution of wet well-fixed cells and reduction in debris and mucus, which will reduce the unsatisfactory smear (8). The technique has higher sensitivity than conventional method in high-risk population (16) and also in population with low incidence (9). The Papsin method, a new liquid-based cytology technique, is cost-effective in cervical cancer screening (20). However, Herbert and Johnson (21) suggested that liquid-based cytology technology need to be further assessed due to its expensive cost in term of equipment, capital cost, maintenance, consumables, training, technical preparation time, transportation and disposal liquid media. Similar view reported by Farnsworth (22) based on an Australian experience.

In conclusion, the adequacy of Pap smear specimen is an important factor for detection abnormal Pap smear results. Effort to obtain satisfactory smears need to be addressed to avoid false negative results, further delaying detection of early cervical cancer. This could be done by improving patient preparation and technique by the health personnel, and considering the used of liquid-based cytology. Further studies with larger sample size which involves several years review, and involving the health personnel skills are needed to look at the association between adequacy of specimen and abnormal results.

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Table 1. Characteristics of clinical summary and Pap smear findings in 238 samples

Variable	n (%)
Methods of contraception	
None	133(55.9)
Hormon	69(29.0)
IUCD	17 (7.1)
Others	19 (8.0)
Hormonal status	
Perimenopause	219(92.0)
Postpartum	12 (5.0)
Menopause	7 (3.0)
Symptom at presentation	
No symptom	231(97.1)
Abnormal bleeding	5 (2.1)
Discharge	2 (0.8)
Condition of cervix at presentation	
Normal	233(97.9)
Abnormal	5 (2.1)
Methods of acquiring sample	
Cervical scrape	116(49.0)
Endocervical brush	6 (2.0)
Both scrape and brush	116(49.0)
Adequacy of specimen	
Satisfactory for evaluation	135(56.7)
Satisfactory but limited by	95(40.0)
Unsatisfactory	8 (3.3)
Pap smear results	
Within normal limit	183(77.0)
BCC due to reactive changes	37(15.5)
BCC due to infection	16 (6.7)
Squamous cell abnormalities	1 (0.4)
Glandular cells abnormalities	1 (0.4)

IUCD Intrauterine Contraceptive Device
BCC Benign Cellular Changes

Table 2. Associated factors for abnormal Pap smear results by univariate analysis

Variable	Pap smear results Mean (SD)		Pap smear results n (%)		*P* value
	Normal	Abnormal	Normal	Abnormal	
Age (year)	34.7(8.1)	35.6(8.2)			0.491*
Parity	4.1(2.4)	4.1(2.3)			0.887 *
Age at marriage (year)	22.5(4.6)	22.4(3.9)			0.488 *
Condition of cervix					
Normal	–	–	180(77.3)	53(22.7)	1.000**
Abnormal			4(80.0)	1(20.0)	
Adequacy of specimen					
Satisfactory	–	–	95(69.3)	42(30.7)	0.001***
Unsatisfactory			89(88.1)	12(11.9)	
Symptom at presentation					
No	–	–	182(78.8)	49(21.2)	0.007**
Yes			2(28.6)	5(71.4)	
Method of contraception					
None	–	–	99(75.0)	33(25.0)	0.037***
IUCD			12(60.0)	8(40.0)	
Hormonal			60(85.7)	10(14.3)	

* Independent t test
** Fisher s Exact test
*** Chi square test

SD Standard Deviation
n Frequency
IUCD Intrauterine Contraceptive Device

Table 3. Associated factors for abnormal Pap smear results by Multiple Logistic Regression

Variable	Crude OR (95% CI for OR)	Adjusted OR (95% CI for OR)	*P* value
Adequacy of specimen			0.001
Unsatisfactory	1	1	
Satisfactory	3.28 (1.62, 6.63)	3.26 (1.59, 6.68)	
Symptom at presentation			0.012
No	1	1	
Yes	9.29 (1.75, 49.32)	9.14 (1.62, 51.47)	

Adjusted for age, parity, age at marriage, condition of cervix and contraceptive used
Specificity=98.9%, sensitivity=9.3%, overall %=78.6%
ROC curve: Area under the curve=0.657 (95% CI: 0.576, 0.738)
p value for Hosmer Lemeshow test: 0.280
OR : Odds Ratio

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