

## ORIGINAL ARTICLE

# CERVICAL CYTOLOGY PATTERNS AT TERTIARY CARE CENTER IN URBAN SETTING OF PAKISTAN

Aaisha Aman<sup>1</sup>, Rubina Hussain<sup>1</sup>

<sup>1</sup> Department of Obstetrics and Gynaecology, Ziauddin University Hospital, Karachi, Pakistan

## ABSTRACT

**Background:** Cervical cancer is regarded as a second most common cancer among women. In developing countries, a disproportionate influence of cervical cancer has accounted approximately 85% of the cases. Identification cytological findings in these women are of utmost importance. Studies reported that proper screening program is not implemented for our population, while the opportunistic contact of women to the doctor can be utilized to screen these females.

**Methods:** This cross-sectional study was carried out at Department of Gynecology and Obstetrics, Ziauddin University and Hospitals from April to September 2016. Total of 370 women age 18-65 years, sexually active were included. Pap smear was taken after taking informed consent. Sample was stored; reports were checked and documented on Performa.

**Results:** The mean age of the patients was  $39.54 \pm 12.9$  years. The mean sexual debut of the patients was  $10.02 \pm 9.8$  years. Squamous cell carcinoma and Intraepithelial lesions were observed in none (0%) of the patients. Atypical squamous cell carcinoma-cannot exclude HSIL was observed in 1 (0.3%), low grade squamous intraepithelial lesions in 2 (0.5%), high grade squamous intraepithelial lesions in 1 (0.3%) while atypical glandular cells not otherwise specified was also observed in 1 (0.3%) patients.

**Conclusion:** The finding of this study has revealed positive cytological findings in five patients. In particular, low grade squamous intraepithelial lesions were found higher followed by high grade squamous intraepithelial lesions, atypical squamous cell carcinoma-cannot exclude HSIL and atypical glandular cells not specified.

**KEYWORDS:** Cervical Cancer, Pap Smear, Squamous Cell Carcinoma

## Corresponding Author

Dr. Aaisha Aman

Department of Obstetrics and Gynaecology,

Ziauddin University Hospital,

Karachi, Pakistan.

Tel: 0333-2448576,

E-mail: aaishaamank@gmail.com

## INTRODUCTION

The Papanicolaou test which is also termed as "Pap test", "cervical smear", "Pap smear", or "smear test" is test used for screening. It helps in identifying the potentially precancerous and carcinomatous processes at the alteration phase in reproductive system of the females which are usually caused by sexually transmitted Human Papilloma Viruses (HPV). The uncommon outcomes are repeatedly

tracked up by the subtler investigative technique. Pap test remains a widely used effective investigative tool for early detection of precancerous and cervical carcinomas<sup>1</sup>. Furthermore, this test can also perceive endocervix infections and its abnormalities.

In case of abnormality, close monitoring is recommended and detailed examination of the cervix by colposcopy could be recommended. The patient

can be referred for "HPV DNA testing", which can serve as an aide to "Pap testing".<sup>1</sup> The guidelines used to screen women may vary one state to other state. However, usually screening start from the age of twenty or twenty-five years and last still round the age of fifty or sixty years.<sup>2</sup>

According to the literature the accuracy of conventional cytology report shows sensitivity-72% and specificity-94%.<sup>3</sup> Other studies on the accuracy of liquid-based-monolayer cytology report shows sensitivity 61%<sup>4</sup> to 66%<sup>3</sup> and-specificity 82%<sup>4</sup> to 91%.<sup>3</sup>

The Bethesda system is used in case of abnormal results. It consists of "Squamous cell abnormalities" (SIL) which includes "atypical squamous cells of undetermined significance" (ASCUS), "atypical squamous cells – cannot exclude HSIL" (ASC-H), "low grade squamous intraepithelial lesion" (LGSIL or LSIL), "high-grade squamous intraepithelial lesion" (HGSIL or HSIL), and "Squamous cell carcinoma". Glandular epithelial cell abnormalities include "atypical Glandular Cells not otherwise specified"(AGC or AGC-NOS).<sup>5</sup> The abnormalities of endometrial and endocervical can also be diagnosed, a number of infectious processes, herpes simplex virus, including yeast and trichomoniasis. Though, it is not very sensitive indistinguishing these infections, there for a negative Pap does not mean no infection.

The rationale of the study was to determine the cervical cytological pattern of various cervical smear abnormalities at our tertiary care center in urban setting of our country, to find out the prevalence of epithelial cell abnormalities and to study the accuracy of Pap smear test by correlating with histopathology. In our country, exact frequency of cytological findings according to age is not known. The proper screening program is not implemented for our population, while the opportunistic contact of women to the doctor can be utilized to screen these females.

## METHODS

This cross-sectional study was carried out at Department of Gynecology and Obstetrics, Ziauddin University and Hospitals from April to September 2016. After approval from the ethical Review committee (ERC) of Ziauddin University Hospital, Karachi, A total of 370 eligible women age 18-65 years, sexually active and fulfilling the inclusion criteria were included. Those women who were pregnant, refused to participate, had normal pap smear or active vaginal bleeding were excluded.

After taken informed consent Pap smear was taken

in OPD by GYNE residents in dorsal position after asking patient to empty urinary bladder, cervix was visualized with help of cuscus speculum pap smear was taken with Ary'spectula from transformation zone of cervix sample was spread on glass slid that was fixed stored and transported in 95% ethyl alcohol bottle, samples were labeled with MR number name was optional. Then reports were checked and documented on Performa.

Data were analyzed using SPSS version 20.0. Descriptive analysis was performed for continuous and categorical variables. Data on continuous variables like age, parity, sexual debut since were presented to mean +SD. Categorical variables like atypical squamous cells of undetermined significance (ASC-US), atypical squamous cells-cannot exclude HSIL (ASC-H), low-grade squamous intraepithelial lesion (LGSIL), high-grade squamous intraepithelial lesion (HGSIL), Squamous cell carcinoma, and atypical epithelial Glandular Cells not otherwise specified (AGC) like Squamous cell presented as percentages. Confounding variables were controlled by stratification at the time of analysis.

## RESULTS

In this study the mean age of the women was 39.5 ±12.9years. There were 215 (58.1%) patients with ≤40 years of age while 155 (41.90%) patients with >40 years of age. Mean parity of the patients was 2.5 ±1.5. There were 118 (31.9%) primiparas, 211 (57%) multiparas and 41 (11.1%) grand multiparous patients. The mean sexual debut of the patients was 10.0 ±9.8 years. Majority of the patients had sexual debut since ≤10 years (n=219, 59.2%) while in 151 (40.8%) patients >10 years since sexual debut was observed. In 233 (63%) patients no miscarriage occurred, while in 91 (24.6%) patients one time and in 46 (12.4%) patients more than two times miscarriage occurred (Table 1).

Squamous cell carcinoma and Intraepithelial lesions were not found (0%) in enrolled women in this study. Atypical squamous cell carcinoma-cannot exclude HSIL was observed in 1 (0.3%), Low grade squamous intraepithelial lesions in 2 (0.5%), High grade squamous intraepithelial lesions in 1 (0.3%) while Atypical glandular cells not otherwise specified was also observed in 1 (0.3%) patients (Table 2).

The comparison was done to see the association of cytological findings with baseline characteristics of the patients. Atypical squamous carcinoma cells were not significantly associated with the women age, parity, sexual debut and miscarriages. Results are shown in Table 3.

TABLE 1: CHARACTERISTICS OF THE WOMEN (N=370)

VARIABLES		N (%)
<b>AGE (IN YEARS)</b>	<b>MEAN <math>\pm</math>SD</b>	39.54 $\pm$ 12.9
$\leq 40$		215 (58.1)
$> 40$		155 (41.9)
<b>PARITY OF THE PATIENTS</b>	<b>MEAN <math>\pm</math>SD</b>	2.52 $\pm$ 1.5
PRIMIPARAS		118 (31.9)
MULTIPAROUS		211 (57.0)
GRAND MULTIPAROUS		41 (11.1)
<b>SEXUAL DEBUT SINCE (IN YEARS)</b>	<b>MEAN <math>\pm</math>SD</b>	10.02 $\pm$ 9.8
$\leq 10$		219 (59.2)
$> 10$		151 (40.8)
<b>MISCARRIAGES</b>		
NONE		233 (63.0)
ONE TIME		91 (24.6)
MORE THAN ONE TIME		46 (12.4)

TABLE 2: FREQUENCY OF CARCINOMA CELLS IN WOMEN (N=370)

CARCINOMA CELLS	YES		NO	
	N	%	N	%
SQUAMOUS CELL CARCINOMA	0	0	370	100
INTRAEPITHELIAL LESIONS	0	0	370	100
ATYPICAL SQUAMOUS CELL CARCINOMA-CANNOT EXCLUDE HSIL	1	0.3	369	99.7
LOW GRADE SQUAMOUS INTRAEPITHELIAL LESIONS	2	0.5	368	99.5
HIGH GRADE SQUAMOUS INTRAEPITHELIAL LESIONS	1	0.3	369	99.7
ATYPICAL GLANDULAR CELLS NOT OTHERWISE SPECIFIED	1	0.3	369	99.7

TABLE 3: COMPARISON OF ATYPICAL SQUAMOUS CELL CARCINOMA-CANNOT EXCLUDE HSIL WITH BASELINE CHARACTERISTICS (N=370)

VARIABLES	ATYPICAL SQUAMOUS CELL CARCINOMA-CANNOT EXCLUDE HSIL		TOTAL	P-VALUE
	YES N(%)	NO N(%)		
<b>AGE (IN YEARS)</b>				
$\leq 40$	1 (0.5)	214 (99.5)	215 (100)	0.395
$> 40$	0 (0)	155 (100)	155 (100)	
<b>PARITY</b>				
PRIMIPARAS	0 (0)	118 (100)	118 (100)	0.685
MULTIPAROUS	1 (0.5)	210 (99.5)	211 (100)	
GRAND MULTIPAROUS	1 (0.3)	40 (99.7)	41 (100)	
<b>SEXUAL DEBUT SINCE</b>				
$\leq 10$	1 (0.5)	218 (99.5)	219 (100)	0.406
$> 10$	0 (0)	151 (100)	151 (100)	
<b>MISCARRIAGES</b>				
NONE	0 (0)	233 (100)	233 (100)	0.029
ONE TIME	0 (0)	91 (100)	91 (100)	
MORE THAN ONE TIME	1 (2.2)	45 (97.8)	46 (100)	

## DISCUSSION

This study was conducted with the aim to determine the cytological findings in Pap smear in individuals in between 18 to 65 years of age group. In this study the mean age of the patients was 40 years. Moreover, the majority of the patients were in reproductive age, i.e. less than equal to 40 years age group. Somewhat alike age distribution was also reported in other studies.<sup>6-9</sup>

In a study conducted by Bal et al.<sup>11</sup> majority of the women were presented in 31-40 years of age group. Another study conducted from Pakistan has reported the mean age of women as 55 years. The status of sexual debut in this study was ranged from 1 year to 51 years. Majority of the patients had less than 10 years of sexual debut. The multiparous status was found higher in this study followed by primiparas. A total of 11 women with grand multiparous were also presented in the study. Similarly, the preponderance of multiparity was also reported in the study of Bukhari et al.<sup>8</sup>

Furthermore, the author also reported the higher frequency of early marriage as well.<sup>8</sup>

Cytological findings of our study have shown that none of the patients were presented with squamous cell carcinoma and Intraepithelial lesions. However, atypical squamous cell carcinoma-cannot exclude HSIL, high grade squamous intraepithelial lesions and atypical glandular cells not otherwise specified was found in one patient each whereas low grade squamous intraepithelial lesions were found in two patients. This finding also matched with the findings of a study in which low-grade squamous cell intraepithelial lesions was found higher followed by high-grade squamous cell intraepithelial lesions. However, contrary to our results, squamous cell carcinoma was also found in their study with the percentage of 13.7%.<sup>8</sup> In another study, low grade squamous intraepithelial lesion was found in eight patients whereas atypical squamous cells of undetermined significance were observed in one patient.<sup>6, 10, 11</sup>

Our study are also in accordance with the findings of Patel et al.<sup>12</sup> and Anuradha et al.<sup>13</sup> Few studies<sup>14-16</sup> have reported a lower rate for squamous intraepithelial lesion.

The comparison of age and sexual debut duration with cytological findings in our study showed that positive atypical squamous cell carcinoma-cannot exclude HSIL, low grade squamous intraepithelial lesion and atypical glandular cells not otherwise specified was found in women with reproductive age group ( $\leq 40$  years age) while high grade squamous intraepithelial lesion was found in older ( $> 40$  years age) women.<sup>16</sup>

The comparison of parity status showed that atypical squamous cell carcinoma-cannot exclude HSIL was found positive in one woman with multiparous and one woman with grand multiparous status, while low grade squamous intraepithelial lesion and high grade squamous intraepithelial lesion was found positive in multiparous women only, i.e.  $n=2$  and 1, respectively. Atypical glandular cells not otherwise specified were found positive in one primipara's woman only.<sup>17-20</sup>

In our study, although more than one miscarriages were found less than 46 (12.4%) as compared to only one miscarriage ( $n=91$ , 24.6%) and none miscarriage (0%). When compared with cytological findings, women having more than one miscarriage were significantly more likely to have atypical squamous cell carcinoma-cannot exclude HSIL. One patient with atypical glandular cells not otherwise specified had no miscarriage history while high grade squamous intraepithelial lesion and low grade squamous intraepithelial lesion had one miscarriage history each. LSIL and HSIL on cytology found to be more prevalent in patients who started sexual activity before 20 years of age.<sup>21-25</sup>

Miscarriage was the only variable found statistically significant with atypical squamous cell carcinoma-cannot exclude HSIL while other variables were insignificantly association with cytological findings.

## CONCLUSION

Cervical cancer is a non ignoring source of death in Pakistan. Our study shows a comparatively low frequency which is comparable to that of developed world. Pap smear testing is easy, very useful, harmless and very economical method to detect pre-invasive cervical epithelial lesions. Government needs to implement in public and private hospitals on routine basis. Woman of above 30 years of age must be subjected to Pap smear and this must be continued even in post-menopausal period to detect abnormality timely. The purpose of our study is that there is requirement to conduct more researches to estimate the outline of cervical cytological abnormalities along with detection of frequent HPV strains in our setup, and this information can be helpful for prevention of HPV infections whichever by vaccines or possible targeted treatment.

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