CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187
http://doi.org/10.5281/zenodo.3975960

Available online at: http://www.iajps.com *Research Article*

A CLINICOPATHOLOGICAL STUDY ON THE SCREENING OF CARCINOMA CERVIX

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Article Received: June 2020 **Accepted:** July 2020 **Published:** August 2020

Abstract:

BACKGROUND: *Cervical cancer, the pathogenesis of which is multifaceted, was the leading cause of death 50 years ago, and mortality has been reduced to two-thirds thanks to successful screening with Pap smears that detected cancer and precancerous conditions.*

Aim: *The study was undertaken to analyze the routine screening for cervical cancer by age and to investigate various predisposing factors for cervical cancer.*

Place and Duration: *In the Obstetric and Gynecology department of Services Hospital Lahore for two-year duration from March 2018 to March 2020.*

Methods: *We conducted an observational study on 1,000 patients. In these patients, cervical smears and predisposing factors were examined.*

Results: *1000 women over 20 years of age were examined. There were 242 cases (24.2%) of dysplasia, including 133 (13.3%) mild dysplasia, 59 cases (5.9%) moderate dysplasia and 50 cases (5%) severe dysplasia. Invasive cancer was found in 29 cases (2.9%). There were 564 (56.4%) inflammatory smears and 168 (16.8%) normal smears. The maximum number of dysplasia's and cancers was found in the age group over 40 years. These patients were from a low-income group, had no formal education, achieved their first menstrual period at the age of 13-14, were married at the age of 15-17, had three or more children, and had been married for over 30 years.*

Conclusion: *Cervical cytology is the main stay in the prevention and early diagnosis of cervical cancer. Due to its simplicity and low cost, pulp swabs can be used for mass screening. Cervical cancer has many etiological factors that play a role in its pathogenesis.*

Key words: *Pap smear, Cervical carcinoma, Cytology, precancerous conditions.*

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Please cite this article in press Sameera Wajahat Rabbani et al, ***A Clinicopathological Study On The Screening Of Carcinoma Cervix.,*** *Indo Am. J. P. Sci, 2020; 07(08).*

INTRODUCTION:

Cervical cancer is the sixth most common celiac cancer in women and is responsible for 5% of all cancer deaths in women worldwide. It accounts for about 15% of all cancers diagnosed in women worldwide. There have been 1.7 million cases of cervical cancer and 5-13 million cases of precancerous lesions in developing countries 2.3. South Africa has the highest severe death rate. In North America, Western Europe and Australia, the incidence of cervical cancer is low. China has the lowest death rate. Cervical cancer mortality has decreased in recent years due to early cancer detection and precancerous conditions. Cervical cancer screening with Pap smears reduced the incidence of cervical cancer by 53%. The high incidence, long detectable preclinical phase and the benefits of early treatment determine the susceptibility of cervical cancer to prophylaxis through a screening program. Pap smear screening, if performed correctly, is sensitive enough and has a high specificity, is cheap and carries a low risk to the patient. Massive Pap smear tests shifted the picture of cervical cancer from clinical to preclinical. Although the incidence of cervical cancer has decreased significantly since 1960, age-dependent rates; however, they show an increase in the number of young women, especially in the 25-29 age group. This is not due to less effective screening of the younger population, but an increase in incidence would be due to a predisposition to risk factors. In this study, we tried to analyze the factors that predispose to cervical cancer and the incidence of cervical cancer by age.

MATERIAL AND METHODS:

This cross-sectional study includes 1,000 patients held in the Obstetrics and Gynecology department of Services Hospital Lahore for two-year duration from March 2018 to March 2020. The institutional ethics committee approved the study protocol. Informed consent was obtained from all study participants. Pap smears were taken from 1,000 patients who were over 20 years of age. Etiological factors and risks were investigated, such as age, delivery, age of first menstruation, age of marriage, use of oral contraceptives, socioeconomic status, and educational status of patients with dysplastic smears. Patients with smears only inflammatory lesions without dysplasia were excluded. Smears were taken from the patients with an Aylesbury spatula. These smears were stained with Papanicolaou dye. The patient was placed in a dorsal or left-sided lithotomy. In order to visualize the cervix, a non-lubricated (self-locking) speculum was inserted into the vaginal opening. The Aylesbury spatula is placed in place and turned clockwise through 3600 to obtain a specimen with ectocervix and endocervix, including squamous cervical junction. The preparation is spread evenly on the slides. The collected smears were fixed in 95% isopropyl alcohol for 15-30 minutes. These smears are stained with Papanicolaou dye. Patient swabs which revealed dysplastic cells on microscopic examination were examined in detail. Patients with the presence of dysplastic cells were examined in detail.

RESULTS:

Cervical smears from 1,000 women over 20 years of age who came to a gynecological clinic were examined, a detailed interview was recorded including age, age of first menstruation, married life, number of pregnancies, age of the last child, duration of menopause, use of oral contraceptive pills (OCP), chewing or smoking tobacco, women's socioeconomic and educational status. The gynecological symptoms and clinical condition of the cervix were also examined. The women were divided into 9 groups depending on their age and various cytological features were examined (Table 1). There were 242 cases (24.2%) of dysplasia, including 133 cases (13.3%) of mild dysplasia, 59 cases (5.9%) moderate, and 50 cases (5%) severe. Invasive cancer was found in 29 cases (2.9%). There were 564 (56.4%) inflammatory smears and 168 (16.8%) normal smears (Table 1).

Table 1: Epithelial abnormalities in relation to age

Age in years	Total	Normal smears	Inflammatory smears	LSIL Mild dysplasia	HSIL Moderate severe dysplasia		Invasive carcinoma
20-30	203 (20.3%)	24 (2.4%)	150 (15%)	25 (2.5%)	2 (0.2%)	2 (0.2%)	-
31-40	304 (30.4%)	53 (5.3%)	187 (18.7%)	36 (3.6%)	14 (1.4%)	11 (1.1%)	3 (0.3%)
41-50	287 (28.7%)	51 (5.1%)	148 (14.8%)	44 (4.4%)	22 (2.2%)	13 (1.3%)	8 (0.8%)
51-60	128 (12.8%)	22 (2.2%)	56 (5.6%)	17 (1.7%)	11 (1.1%)	14 (1.4%)	9 (0.9%)
61 and above	78 (7.8%)	15 (1.5%)	23 (2.3%)	11 (1.1%)	10 (1%)	10 (1.0%)	9 (0.9%)

The highest incidence of mild and moderate dysplasia was recorded in the 40-50 age group. Severe dysplasia and cancers have been observed in the 50-60 age group. In the age group of 20–30 years, one case of invasive cancer was reported (Table 1). The maximum cases of invasive cancer, mild dysplasia, moderate and severe dysplasia were reported in the menopausal age group compared to the reproductive age group (Table 2).

Table 2: Epithelial abnormalities in menopausal and reproductive age group women

Age groups	Total	Normal smears	Inflammatory smears	LSIL mild dysplasia	HSIL Moderate Severe dysplasia		Invasive carcinoma
Menopausal	449 (44.9%)	90 (9%)	192 (19.2%)	73 (7.3%)	37(3.7%)	33 (3.3%)	24 (2.4%)
Reproductive	551 (55.1%)	75 (7.5%)	372 (37.2%)	60 (6%)	22(2.2%)	17 (1.7%)	5 (0.5%)

Epithelial lesions were examined depending on age at the time of the first menstruation, with the highest incidence of dysplasia reported in patients with the first menstruation at the age of 13, and in invasive cancer in patients with their first menstruation at the age of 14 (Table 3).

Table 3: Epithelial abnormalities in relation to age at menarche

Age at menarche in years	Total	Normal smears	Inflammatory smears	LSIL mild dysplasia	HSIL Moderate severe dysplasia		Invasive carcinoma
10-11 Years	40 (4%)	4 (0.4%)	24 (2.4%)	2 (0.2%)	5 (0.5%)	-	5 (0.5%)
12 years	276 (27.6%)	38 (3.8%)	153 (15.3%)	43 (4.3%)	17 (1.7%)	21 (2.1%)	4 (0.4%)
13 years	418 (41.8%)	69 (6.9%)	230 (23%)	64 (6.4%)	25 (2.5%)	23 (2.3%)	7 (0.7%)
14 years	185 (18.5%)	39 (3.9%)	114 (11.4%)	13 (1.3%)	7 (0.7%)	3 (0.3%)	9 (0.9%)
15 years and above	81 (8.1%)	15 (1.5%)	43 (4.3%)	11 (1.1%)	5 (0.5%)	3 (0.3%)	4 (0.4%)

When the incidence of dysplasia was examined by age at the time of marriage, the highest incidence of moderate to severe dysplasia and cancer was found in married patients aged 15-17 years (Table 4).

Table 4: Epithelial abnormalities in relation to age at marriage

Age at marriage	Total	Normal smears	Inflammatory smears	LSIL Mild dysplasia	HSIL Moderate severe dysplasia		Invasive carcinoma
10-14 yrs	151 (15.1%)	31 (3.1%)	69 (6.9%)	21 (2.1%)	16 (1.6%)	8 (0.8%)	6 (0.6%)
15- 17 yrs	406 (40.6%)	50 (5.0%)	210 (21 %)	55 (5.5%)	33 (3.3%)	39 (3.9%)	19 (1.9%)
18yrs and above	443 (44.3%)	84 (8.4%)	285 (28.5%)	57 (5.7%)	10 (1 %)	3 (0.3%)	4 (0.4%)

The incidence of cancer was found to be high in patients who had a married life of 31 years or more (Table 5).

Married life	Total	Normal smears	Inflammatory smears	LSIL mild dysplasia	HSIL Moderate severe dysplasia		Invasive carcinoma
0-5 years	41 (4.1%)	7 (0.7%)	30 (3%)	4 (0.4%)	-	-	-
6-10 years	93 (9.3%)	18 (1.8%)	58 (5.8%)	15 (1.5%)	2 (0.2%)	-	-
11-20 years	267 (26.7%)	31 (3.1%)	187 (18.7%)	32 (3.2%)	5 (0.5 %)	10 (1%)	2 (0.2%)
21-30 years	285 (28.5%)	48 (4.8%)	165 (16.5%)	37 (3.7%)	19 (1.9%)	13 (1.3%)	3 (0.3%)
31 years and above	314 (31.4%)	61 (6.1%)	124 (12.4%)	45 (4.5%)	33 (3.3%)	27 (2.7%)	24 (2.4%)

A study of the number of deliveries in these patients showed that the highest incidence of invasive cancer, moderate and severe dysplasia was reported in women who had three or more children. In nulliparous women, mild dysplasia was found only in three cases, but there were no cases of moderate, severe dysplasia and invasive cancer (Table 6).

Table 6: Epithelial abnormalities in relation to parity

Parity	Total	Normal smears	Inflammatory smears	LSIL mild dysplasia	HSIL Moderate severe dysplasia		Invasive carcinoma
0	56 (5.6%)	22 (2.2%)	31 (3.1%)	3 (0.3%)	-	-	-
1	83 (8.3%)	17 (1.7%)	51 (5.1%)	11 (1.1%)	1 (0.1%)	3 (0.3%)	-
2	368 (36.8%)	53 (5.3%)	240 (24%)	53 (5.3%)	11 (1.1%)	8 (0.8%)	3 (0.3%)
3and above	493 (49.3%)	73 (7.3%)	242 (24.2%)	66 (6.6%)	47 (4.7%)	39 (3.9%)	26 (2.6%)

Epithelial abnormalities were also examined depending on economic status, which showed that the incidence of dysplasia and invasive carcinomas was maximum in the lower income group (Table 7) and they had no formal education (Table 8).

Table 7: Epithelial abnormalities in relation to economic status

Economic status	Total	Normal smears	Inflammatory smears	LSIL mild dysplasia	HSIL Moderate severe dysplasia		Invasive carcinoma
Lower income group	701 (70.1%)	119 (11.9%)	374 (37.4 %)	83 (8.3%)	50 (5%)	47(4.7%)	28 (2.8%)
Middle income group	289 (28.9%)	42 (4.2%)	185 (18.5%)	49 (4.9%)	9 (0.9%)	3 (0.3%)	1 (0.1%)
Upper inco me group	10 (1%)	4 (0.4%)	5 (0.5%)	1 (0.1%)	-	-	-

The majority of patients with dysplasia experienced irregular vaginal bleeding and invasive cancers as postmenopausal bleeding (Table 9).

Table 8: Epithelial abnormalities in relation to education status

Education status	Total	Normal smears	Inflammatory smears	LSIL mild dysplasia	HSIL Moderate severe dysplasia		Invasive carcinoma
No Formal education	665 (66.5%)	103 (10.3%)	345 (34.5%)	88 (8.8%)	52(5.2%)	50 (5%)	27 (2.7%)
Primary education	279 (27.9%)	51 (5.1%)	180 (18%)	39 (3.9%)	7 (0.7%)	-	2 (0.2%)
Higher education	56 (5.6%)	11 (1.1%)	39 (3.9%)	6 (0.6%)	-	-	-

In the clinical trial, mild to moderate cases of dysplasia presented as erosions of the cervix, where cases with severe dysplasia and cancer presented as growths on the cervix or bleeding on the touch (Table 10). considered as risk factors, in our study it did not reveal any significant correlation (Table 11).

Table 9: Epithelial abnormalities and gynecological symptoms

Clinical symptoms	Total	Normal smears	Inflammatory smears	LSIL Mild dysplasia	HSIL Moderate severe dysplasia		Invasive carcinoma
Leucorrhoea	307 (30.7%)	16 (1.6%)	219 (21.9%)	56 (5.6%)	13(1.3%)	2 (0.2%)	1 (0.1%)
Dysuria	35 (3.5%)	8 (0.8%)	24 (2.4%)	3 (0.3%)	-	-	-
Irregular vaginal bleeding	192 (19.2%)	15 (1.5%)	90 (9%)	31 (3.1%)	25(2.5%)	24(2.4%)	7 (0.7%)
Post menopausal bleeding	71 (7.1%)	1 (0.1%)	13 (1.3%)	8 (0.8%)	8 (0.8%)	22(2.2%)	19 (1.9%)
Pain in Lower abdomen	194 (19.4%)	41 (4.1%)	121 (12.1%)	23 (2.3%)	8(0.8%)	1 (0.1%)	-
Mass per vagina	78 (7.8%)	25 (2.5%)	39 (3.9%)	7 (0.7%)	5(0.5%)	-	2 (0.2%)
Routine check up	123 (12.3%)	59 (5.9%)	58(5.8%)	5 (0.5%)	-	1 (0.1%)	-

Table 10: Epithelial abnormalities in relation to clinical lesions

Clinical lesions	Total	Normal smears	Inflammatory smears	LSIL mild dysplasia	HSIL Moderate severe dysplasia		Invasive carcinoma
Erosion cervix	230 (23%)	6 (0.6%)	137 (13.7%)	55 (5.5%)	19 (1.9%)	13 (1.3%)	-
Hypertrophied cervix	63 (6.3%)	10 (1%)	34 (3.4%)	12 (1.2%)	5 (0.5%)	1 (0.1%)	1 (0.1%)
Suspicious cervix (growth/ bleeding on touch)	82 (8.2%)	-	3(0.3%)	10(1%)	10 (1%)	32 (3.2%)	27 (2.7%)
Senile vaginitis	41 (4.1%)	9 (0.9%)	22 (2.2%)	4 (0.4%)	4 (0.4%)	2 (0.2%)	-
Polyp	4 (0.4%)	1 (0.1%)	2 (0.2%)	1 (0.1%)	-	-	-
Endocervicitis	155 (15.5%)	5 (0.5%)	123 (12.3%)	18 (1.8%)	8 (0.8%)	1 (0.1%)	-
Prolapsed	87(8.7%)	29(2.9%)	40 (4%)	12(1.2%)	5(.5%)	-	1 (0.1%)
Normal	338 (33.8%)	105(10.5%)	203 (20.3%)	21 (2.1%)	8 (0.8%)	1 (0.1%)	-

Table 11: Epithelial abnormalities in relation to risk factors

Risk factors	Total	Normal smears	Inflammatory smears	LSIL mild dysplasia	HSIL Moderate severe dysplasia		Invasive carcinoma
Cigarette smoking	-	-	-	-	-	-	-
Tobacco chewing	105(10.5%)	16 (1.6%)	41 (4.1%)	18 (1.8%)	12 (1.2%)	10 (1%)	8 (0.8%)
Immunosuppressive drugs	1 (0.1%)	1 (0.1%)	-	-	-	-	-

DISCUSSION:

The etiology of cervical cancer, which is considered the third most common cancer in women, has been studied epidemiologically for over 150 years. From an epidemiological point of view, cervical cancer behaves like a sexually transmitted disease and is more common in women who have multiple sexual partners or whose partners are promiscuous and not virgins. Epidemiological data have shown that cervical cancer is caused by a sexually transmitted factor, human papillomavirus (HPV), which plays an important role in oncogenesis. Although HPV is considered an important etiological factor, the presence of other risk factors along with HPV infection is important in deciding on disease outcome, ie whether HPV infection will regress or progress to cervical cancer. The USPSTF (US Preventive Services Task Force) recommended that women between the ages of 21 and 65 should undergo Pap smear tests every 3 years. If women (30 to 65 years old) wish to extend the intervals between Pap smears, a combination of Pap smear and HPV testing every 5 years is recommended. The UPSTF does not recommend screening for cervical cancer in women under 21 years of age, women over 65 years of age with normal Pap smears, women who have undergone hysterectomy with cervical removal without previous precancerous lesions or tumors, and testing for the virus HPV. alone or together with cytology in women under 30 years of age. Most of the patients admitted to the hospital belonged to a low socio-economic group. Low, middle- and high-income groups differ in various aspects such as nutritional and vitamin deficiencies, number of births, married life, and age at marriage. Hence, the socio-economic group is an indicator of all of the above factors that contribute to the genesis of cervical cancer. The incidence of invasive cancer in our study was 2.9%, which coincided with the results of JS Misra (2001). In our study, severe dysplasia and invasive cancers were common after 50 years due to the hormonal imbalance that usually occurs in the female reproductive organs. Many factors can play a role and contribute to cancer formation, such as prolonged sex life, multiple sexual partners, childbirth, low socioeconomic status, viral infections, and genetics. It has been found that immunosuppression is associated with dysplastic changes in the cervix. HPV DNA is detected more frequently in pregnant women who experience a transient depression of cellular immunity. More recently, an increased risk of cervical cancer has been observed in HIV patients. Immunosuppression is believed to inhibit papillomavirus clearance and promote its reactivation. Most overt invasive cancers presented as growths on the cervix or cervix that bleed when touched, also found in the JS Misra study. Many cases of dysplasia present as a cervical erosion. Other symptoms include leucorrhoea, bizuria, irregular vaginal bleeding, pain in the lower abdomen, and vaginal lesions. For the prevention of cervical cancer and precursor lesions, the American Cancer Society (ACS) recommends human papillomavirus vaccines for women 11 to 12 years of age. It also suggests that women as young as 9 may be infected with HPV. For women aged 13 to 18 years, immunization against HPV should be given to catch up with vaccinations or to complete the series of vaccinations. Vaccinations are not recommended for women over the age of 26 as it would be best if vaccinated before exposure to genital HPV as the benefits are likely to diminish as the number of sexual partners increases throughout life. Cervical intraepithelial neoplasia and cancer screening should continue even after vaccination. Two prophylactic HPV vaccines are available, namely Gardasil, which protects against HPV types 6, 11, 16, and 18 (tetravalent) and Cervix, which protects against types 16 and 18 (bivalent).

CONCLUSION:

Cervical cancer is not caused by a single etiological factor, but by many independent risk factors, such as age, age of first menstruation, age of marriage, childbirth, educational and economic status, use of oral contraceptives, and smoking all play a role in pathogenesis. Due to the simplicity, low cost, and validity of cytology screening, it becomes clear that this test can be effectively used to detect early cancer and precancerous lesions of the cervix.

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