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Cytological Pattern of Cervical Papanicolaou Smear According to 2014 Bethesda System: A Study Conducted in Tertiary Care Central India, Indore

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Introduction

Cervical cancer ranked second among most commonly diagnosed cancer and in less developed countries it is third leading cause of cancer related death among females[1,2,3] It is estimated that each year, 527,000 new case occur and 275, 000 deaths. Globally, 15% of all cancer in females is cervical cancer.[2,4]. In India about 20% of all cancer related deaths is due to cervical cancer in women and is the number one cause of death in middle aged Indian women.[5] Also, India has 432.20 million women at risk for cervical cancer, annual number of cervical cancer cases is 122,844, annual number of deaths is 67, 4773.[6]

Cancer cervix is a multifactorial disease. Major risk factors are age[7,8], illiteracy, low socioeconomic status, early menarche, marital status, early marriage, early first childbirth, age at last child birth, multiparity, abortion, multiple sexual partners, late menopause, genital infection, poor genital hygiene, tobacco use, passive smoking and contraceptive use [9-13]. Other risk factors includes co-infection with Chlamydia trachomatis, non-use of condoms by partners and nutritional factors.[14-19]

Human Papilloma virus (HPV) infection is the most important risk factor.[20] It has been shown recently that cervical cancer is strongly associated with the presence of high risk or oncogenic Human Papilloma virus (HPV) types (up to 100%).[21,22]

Cervical cancer is a potentially a preventable disease through early detection using several screening techniques.[23] Therefore, the main focus is on the secondary prevention through early detection which is mainly done by cytology. This will lead to treatment of precancerous lesion itself before cancer develops hence reducing the incidence of cervical cancer.[24] In Screening by cytology we look for pre- cancerous changes in the cervix that could develop into cervical cancer.[3] Cytomorphologically abnormal epithelial cells are best demonstrated by the Papanicolaou test. The initial and most important step in cervical cancer screening was the introduction of Papanicolaou (Pap) testing[25,26]. The 2014 Bethesda System has been introduced recently, which is used for reporting cervical smear in our study.

Materials and Methods

This study was conducted in Department of Pathology, Mahatma Gandhi Medical College and Maharaja Yeshwant Rao Hospital, Indore, Madhya Pradesh, India. It is a prospective study. The study duration was one year from July 2017 to June 2018 Sample size for the study was of 40 cases.

Inclusion Criteria

- Symptomatic Females after puberty having following signs and symptoms.
- ❖ Signs and symptoms to be screened: as documented by FIGO (2009) [11]
- Abnormal vaginal bleeding, such as bleeding after vaginal intercourse, bleeding after menopause, bleeding and spotting between periods, and having (menstrual) periods that are longer or heavier than usual. Bleeding after douching or after a pelvic exam may also occur.
- Pain in the lower abdomen or pelvic region.
- An unusual discharge from the vagina − the discharge may contain some blood and may occur between your periods or after menopause.
- Pain during intercourse.
- Any cervical mass seen per speculum, per vaginum or on radiology.
- All the patients who are at risk of cervical cancer attending the gynecology OPD routinely.

Exclusion Criteria

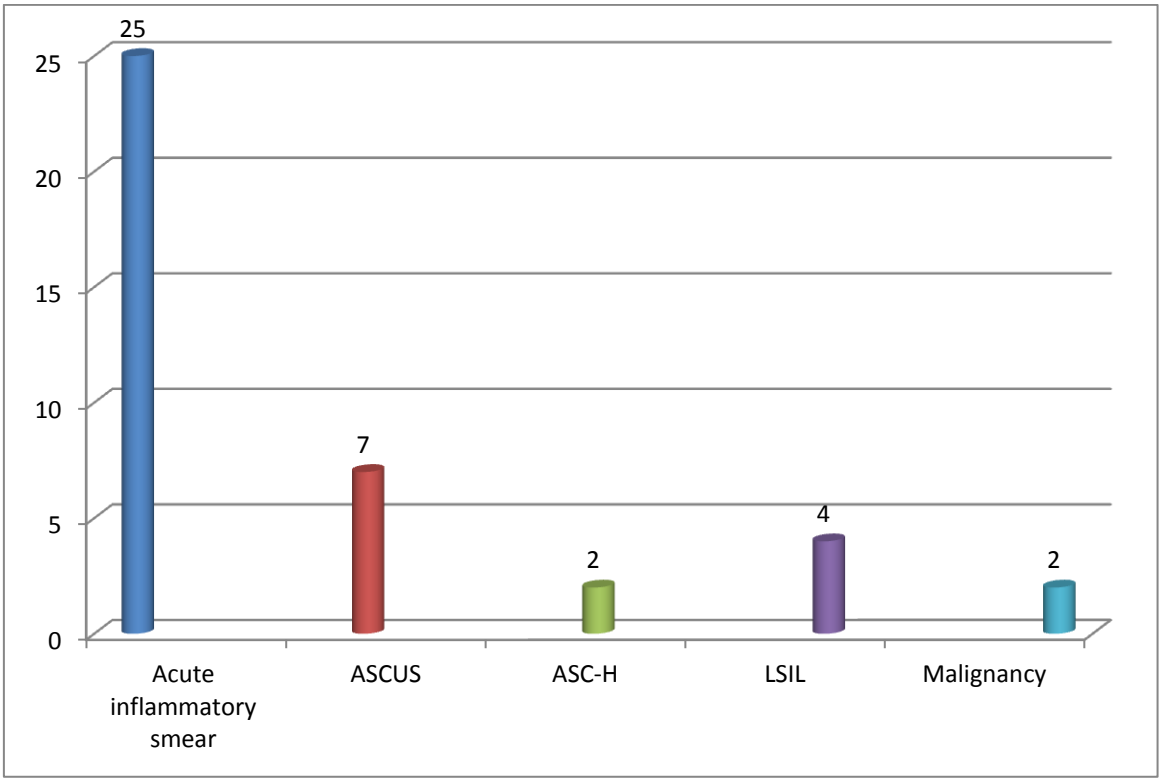
- Females bleeding per vaginum at the time of procedure.
- Patients who have used vaginal medication, vaginal contraceptives, or douches for 48 hours before the sample collection.
- Women who have had their uterus and cervix removed in a hysterectomy.
- Females who were pregnant at the time of screening.
- Patients who have had intercourse the night before the appointment should be avoided.
- Already diagnosed cases of cervical cancer by histopathology.
- All 40 selected women were examined per vaginally and by speculum after acquiring a detailed history and verbal consent from them. The woman was placed in dorsal lithotomy position. After proper positioning of the woman, cervix was viewed by introducing Sims' vaginal speculum and anterior vaginal retractor and external os was identified. Pap smears were made by introducing cervical brush/ cytobrush with a detachable head were inserted into the external os and rotating it through 360 degrees 8-10 times in clockwise direction near the squamo- columnar junction. The cellular material thus obtained was quickly, but gently smeared on a clean glass slide. The glass slide was then immediately put into the Coplin jar containing 95% ethanol which acted as a fixative. The prepared smears were then stained according to Papanicolaou's technique.
- After staining, slides were mounted, screened under light microscope, and reported according to 2014 Bethesda system.

Results & Observation

1. Distribution of benign lesion and epithelial cell abnormalities

Pap smear	No of.cases	%
Total smear	40	100
Inflammatory smear	25	62.5
Epithelial cell abnormality	15	37.5
Atypical epithelial cells Of -Atypical squamous cells undetermined significance [ASCUS]	7	17.5
Atypical squamous cells Cannot exclude HSIL (ASC-H)	2	5
Low grade squamous intraepithelial lesion (HPV/mild dysplasia /CIN I [LSIL]	4	10
Malignancy	2	5

Table No. 1 shows that in the present study, 40 pap smears were analyzed showing the distribution pattern of various condition. Out of which Acute inflammatory smear is 25 (62.5%) and epithelial cell abnormality comprises 15 cases (37.5%).

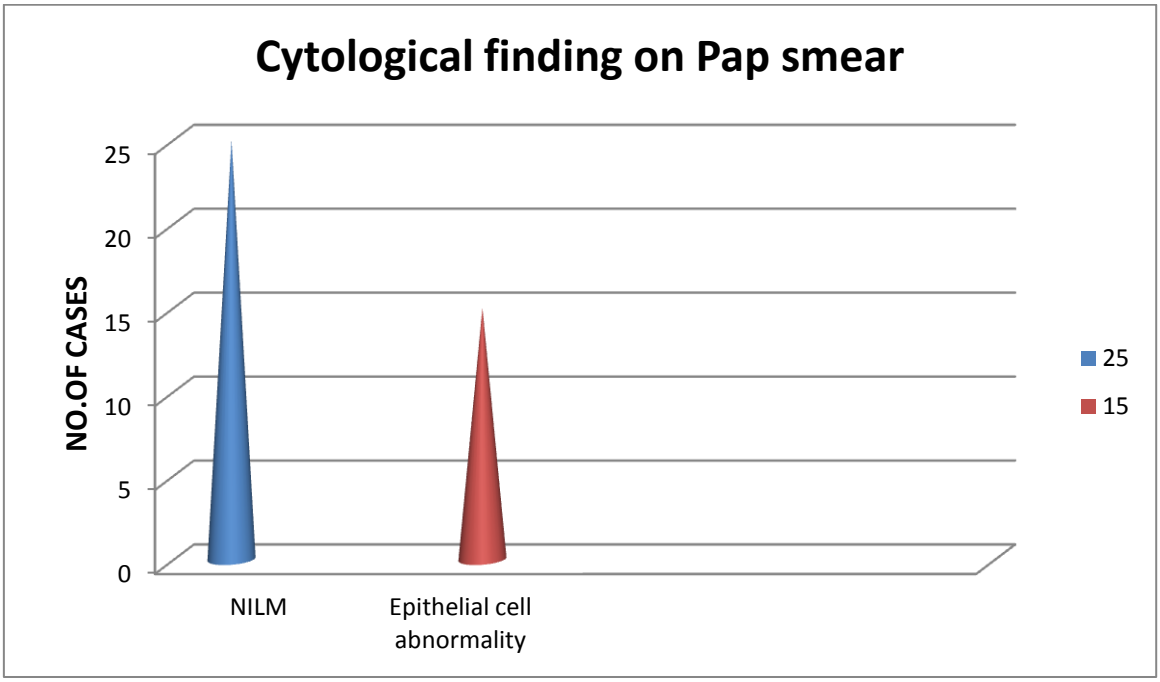


Graph 1- Analysis of pap smear

Table 2 Distribution of Benign lesions and Epithelial cell abnormality

Cytological findings	No. of cases	Percentage%
Negative for intraepithelial lesion or malignancy	25	62.5
Epithelial cell abnormality	15	37.5
Total	40	100.00

Table 2 shows in the present study epithelial cell abnormality is 37.5%.

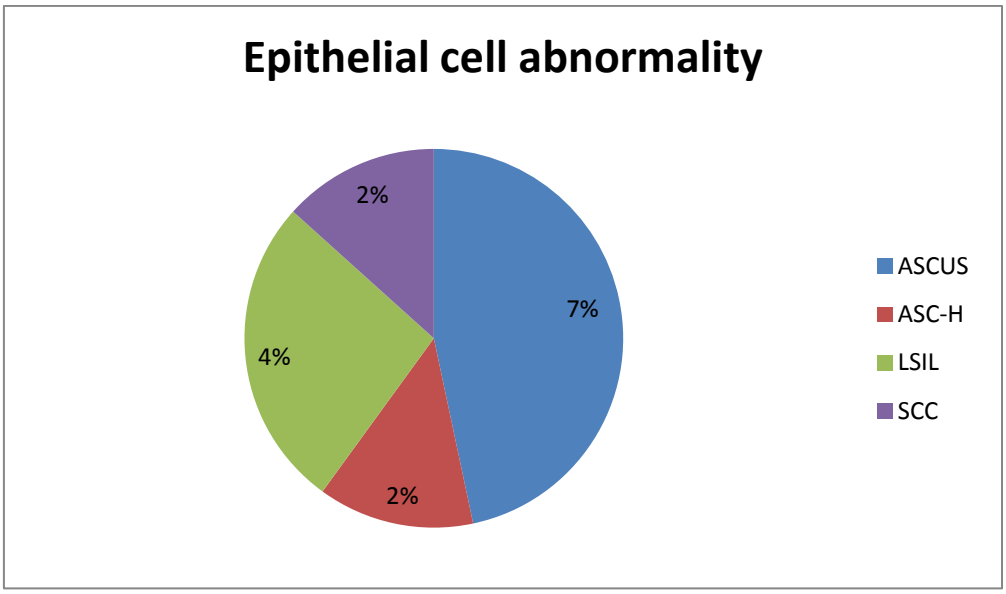


Graph 2 Distribution of NILM and Epithelial cell abnormality.

3. Distribution of epithelial cell abnormality

Epithelial cell abnormality	No. of cases N= 15	Percentage %
ASC-US	07	46.66
ASC-H	02	13.33
LSIL	04	26.66
SCC	02	13.33

Table No 3 shows out of 15 cases of epithelial cell abnormality, 7 cases show Atypical squamous cells of uncertain significance, 2 cases show Atypical squamous cells of uncertain significance cannot exclude HSIL, 4 cases shows low grade squamous intraepithelial lesions. A total of 2 cases show invasive carcinoma cervix.



Graph 3 - Distribution of epithelial cells abnormalities

4. Age distribution of the patients having epithelial cell abnormality

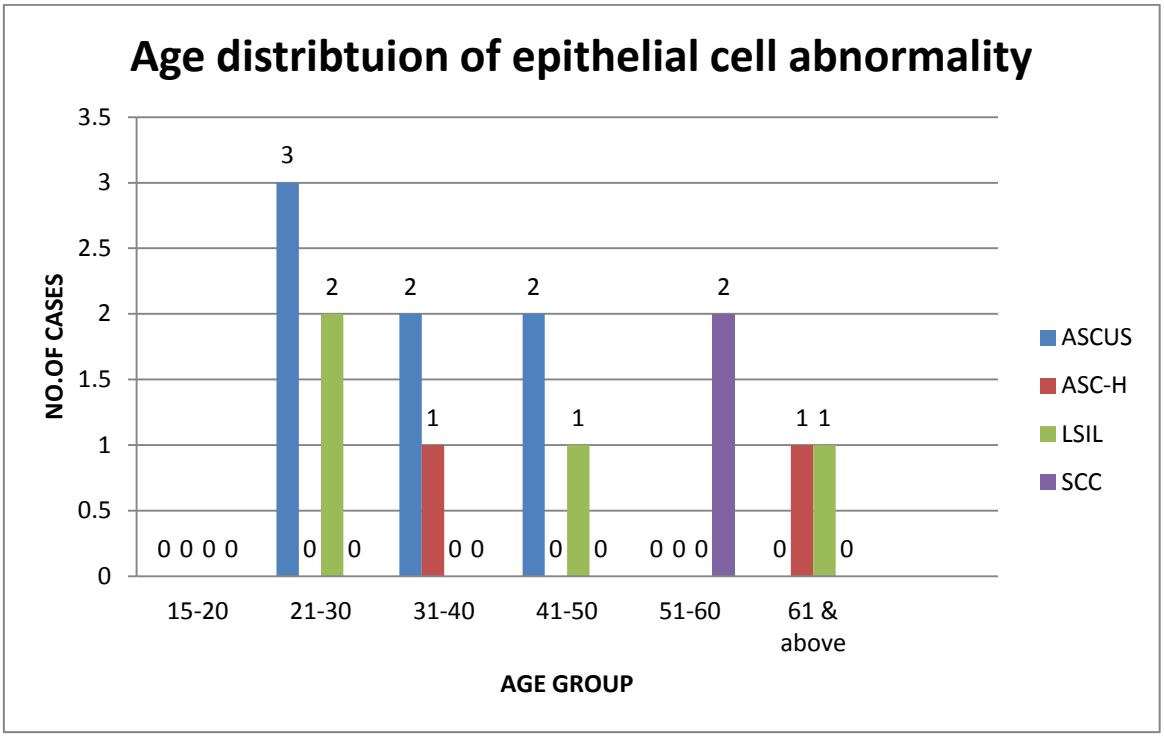
Age (years)	Total cases	NILM	Epithelial cell abnormalities
15-20	02	02	00
21-30	21	16	05
31-40	08	05	03
41-50	05	02	03
51-60	02	00	02
61 and above	02	00	02

Table No. 4 shows that the bulk of patient belong to age group 21-40 years 29 (72.5%).

5. Age distribution in relation to ASCUS,ASC-H, LSIL and SCC

Age (years)	ASCUS n = 7	%	LSIL n = 4	%	ASC-H n = 2	%	SCC n = 2	%
15-20	0	-	0	-	0	-	0	-
21-30	3	42.8	2	50	0	-	0	-
31-40	2	28.6	0	-	1	50	0	-
41-50	2	28.6	1	25	0	-	0	-
51-60	0	-	0	-	0	-	2	100
61and above	0	-	1	25	1	50	0	-

Table no. 5 shows that maximum cases of LSIL were detected in 21-30 years of age group and whereas maximum cases of carcinoma cervix were detected in 51-60 years of age group.

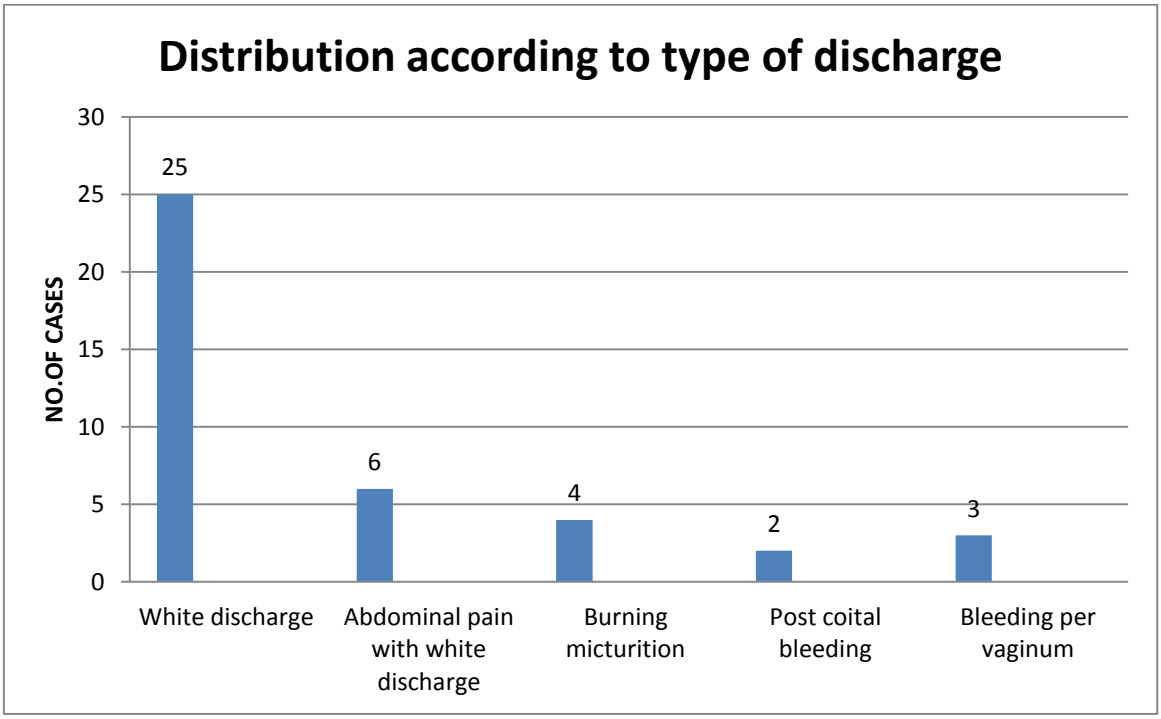


Graph 5 Age distribution of epithelial cell abnormality

6. Distribution of patients according to the complaints for which they visit the clinic

Presenting complaints	No. of patients	Percent (%)
White discharge	25	62.5
Abdominal pain with white discharge	6	15
Burning micturition	4	10
Post coital bleeding	2	5
Bleeding per vaginum	3	7.5

Table no. 6 shows Maximum patients 25 [62.5%], have complaints of white discharge per vaginum



Graph 6 Distribution of patients according to complaints for which they visit

7. Distribution of the epithelial cell abnormalities in association with the presenting complaints

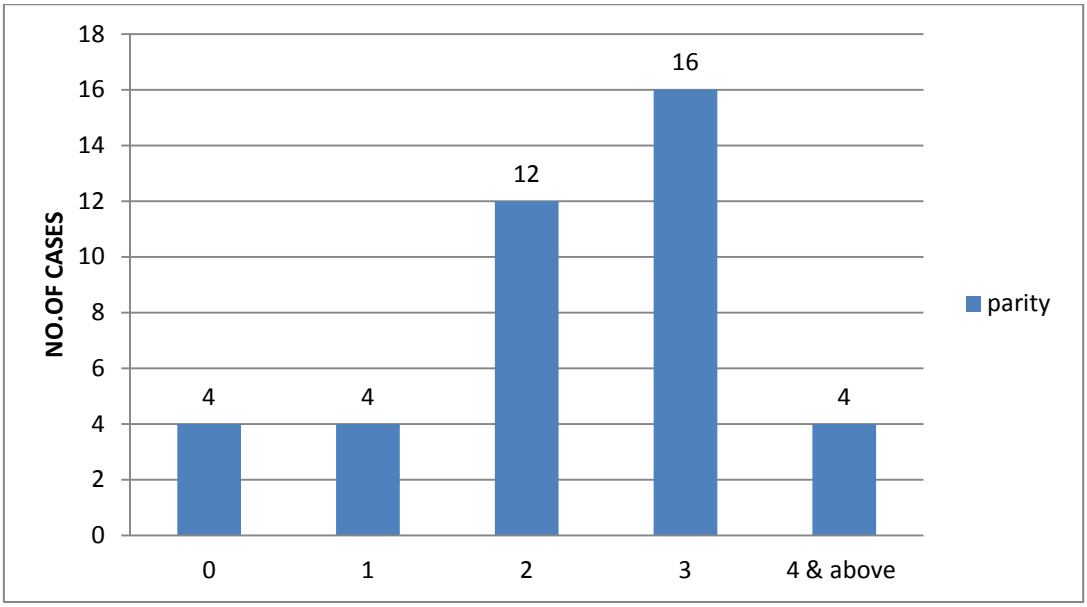
Epithelial cell abnormality	ASCUS N =7	%	ASC-H N= 2	%	LSIL N= 4	%	SCC N= 2	%
White discharge	5	71.4	1	50	3	75	0	-
Abdominal pain with white discharge	0	-	1	50	0	-	0	-
Burning micturition	0	-	0	-	0	-	0	-
Post coital bleeding	1	14.3	0	-	1	25	0	-
Bleeding per vaginum	1	14.3	0	-	0	-	2	100

Table no.7, shows that 75% of patient of LSIL presented with white discharge and rest presented with post coital bleeding. While 71.4% patient of ASCUS presented with white discharge and rest presented. 100% cases of carcinoma cervix presented with the complaint of bleeding per vaginum. However, many patients presented with more than one complaint.

8. Distribution of patients according to parity

Parity	No. of cases	Percentage
0	04	10
1	04	10
2	12	30
3	16	40
4 and above	04	10
Total	40	100

Table No 8, shows that of out of 40, maximum patients belongs to the parity 2 and above.



Graph 8 shows distribution according to parity.

9. Relation of parity with epithelial cell abnormalities

Epithelial cell abnormality / Parity	ASCUS	ASC-H	LSIL	SCC	TOTAL
0	0	0	0	0	0
1	0	0	0	0	0
2	3	0	2	0	5
3	4	1	2	2	9
4 and above	0	1	0	0	1

Table no. 9 shows that significant number of abnormal smear mainly in patients with parity 2 and above.

Discussion

The present study comprised of taking cervical samples of 40 symptomatic women attending the outpatient department of Obstretric & Gynaecology.

Our study revealed ASCUS (17.5%) to be the most common epithelial cell abnormality. Similar results were obtained in other studies which also concluded that ASCUS to be the most common epithelial cell abnormality[27,28]. ASCUS progresses to LSIL, HSIL and SCC. AGUS progresses to adenocarcinoma.[29,30]

Table No. 4 shows that the bulk of patient 29 (72.5%) belong to age group 21-40 years.

Table no. 5 shows that low grade squamous intraepithelial lesion (LSIL) was found in 4 cases (10.0%). It was mainly in the age group 21-30 years. Invasive carcinoma cervix was found in 2 cases (5.0%). It was mainly in the age group 51-60 years. Age incidence of epithelial cell abnormality by various authors-

AUTHORS	AGE (in years)
Sunita A. Bamanikar et.al. [31] (2014)	20-75 years
Hemali J. Tailor et.al. [32] (2016)	25-70 years
Present series 2018	LSIL (21-30 yr) SCC (51-60 yr)

The difference in the age incidence of intraepithelial lesions and carcinoma cervix could be due to wide variation in selection criteria.

Table no. 6, As per as the patients presenting complaint was concerned, white discharge was commonest (62.5%) followed by lower abdominal pain (15.0%), burning micturition (10%), bleeding per vaginum (7.5%) and post coital bleeding (5.0 %).

Commonest complaints by various authors in previous studies-

Author	year	Total no. of cases	Commonest complaints
Aikat et.al. [33]	1974	19574	Asymptomatic (50%)
Juneja et al. [34]	1993	67000	Bleeding P/V (65%)
Manika Alexander [35]	2015	800	White discharge (72%)
Our study		40	White discharge (62.5%)

Table no. 8 shows that maximum number of patients belong to parity group 2 and above. Table no. 9 shows that woman with parity 2 or more are at higher risk of developing squamous intraepithelial lesions and carcinomatous changes. Shrivastav P et.al.[36] (1986) Abnormal cytology was detected in 3.6% of the women in study group (gravid 3 para2 or more), which was significantly higher than the control (gravid 2 para1), indicating that the former are at higher risk of developing cervical cancer. Juneja A.[37] (1993), high incidence of cervical carcinoma in women with parity>2 was noted. Mishra NK et.al.[38] shows that higher parity groups (4 and above) had greater incidence of invasive carcinoma(6.7%) than those of lower parity groups (1.8%). Manika Alexander[39] (2015) showed that intraepithelial lesions and malignancy are Nulliparous 19.9% and Multiparous 80.1%. Women with large number of pregnancies usually start sexual life early and the early age of first intercourse might be etiologically more important than number of pregnancies. The period of early squamous metaplasia is the time of greatest risk for cellular transformation and for the development of cervical neoplasia. Early squamous metaplasia is most frequent in puberty, early adolescence and first pregnancy. Therefore, women who begin sexual activity at an early age when the metaplastic process is most active would have a greater chance of developing cervical cancer.

In nulliparous women, cervical neoplasia is not very common. Hence multiparity is a high risk factor for the development of premalignant and malignant lesions, because of chronic infection, repeated birth trauma, poor personal care, poor nutrition and hygiene etc. Early marriages are still common in our country and hence exposure to coitus and repeated child births at an early age are also common. High parity usually means a young age at marriage and first pregnancy.

One of the significant discrepancies between our study and the previously published data from other countries is the higher rate of ASCUS and lower rate of LSIL. We assume that as the women included in our study were routinely screened

and/or re-screened, they presented with an early form of cytological interpretation in the cervical smear, and thus, ASCUS rate was higher. Most common age to develop carcinoma cervix is between 51-60 years and the precursor lesions occur 5 - 10 years prior to developing invasive cancer. So a test which is detecting more women who are at risk for cervical carcinogenesis should be started as screening test so to drop down the incidence of deadly cervical cancer.

Conclusion

Cervical cytology is method for early detection of intraepithelial lesions and malignancy and therefore should be established as a routine diagnostic aid. The study reveals that the cases of cervical cancer can be detected at early stage if there are proper education and awareness in the society.

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