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Cytohistopathological Correlation of Cervical Lesions

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Abstract: ***Background: Conventional cervical cytology is the most widely used ervical cancer screening test in the world. Squamous intraepithelial neoplasia (SIL) and cervical cancer remain important health problems for women worldwide. Aim and Objective: To study various types of cervical lesions with relevant factors such as age, parity, to classify cervical lesions into malignant & benign groups and to correlate the cytological with histopathological findings. Materials and Methods: This study was conducted on 1065 cases of Pap smears and cervical biopsies, along with resected specimens. After fixation and staining, smears and cervical biopsies were processed and examined under microscope. Results: Maximum number of patients was more than 60 years in age (36.50%)The mean age among cancer cases (51.94±12.30 years) was higher than in cases (39.53±9.66 years) who did not have cervical cancer. Association between age group of cancerous patients and non-cancerous patients were highly significant with pvalue<0.001. Maximum no. of malignancy cases reported in parity 3 (284 cases) followed by parity 4 (212 cases) and minimum cases of cervical cancer were found in parity 1 (40 cases) Maximum number of patients(72%) presented within 1 year of presentation of clinical symptoms consistent with cervical lesions followed by 1-3 years (14%). Majority of patients (60%) presented with abdominal pain followed by vaginal discharge (58%) followed by irregular vaginal bleeding (47%). On cytological examination 50% cases among study population were inflammatory smears and frank malignancy was reported in 17.5% cases, LSIL and HSIL was reported in 8% and 11% respectively. Maximum number of cases on biopsy were those of infections (60.50%), Squamous intraepithelial lesions were seen in 17% patients. Similar cases were those of frank malignancy with benign lesions comprising of only 5% in study population. Out of 605 inflammatory lesions maximum cases were those of chronic cervicitis (94.21% cases) and minimum cases were that of chronic cervicitis with squamous metaplasia (2.47% cases). Most common diagnosis being infection which came out to be 450 cases on cytological examination and 605 cases on histopathological examination, which came out to be non significant with p-value of 0.012, invasive squamous cell carcinoma (17.5%) in both cytological and histopathological findings was also found to be non-significant with the p-value of 0.954.Benign lesions accounted for 325 cases in cytology while 220 cases were diagnosed as benign in histopathology. Which were significant with a p-value of 0.001. Conclusion: Pap smear followed by cervical biopsy is an effective method for detection of pre-cancerous, cancerous and non-cancerous changes in the cervix.***

Keywords: malignant, cervical cancer, pap smear, cervical biopsy

1. Introduction

The cervix is the elongated fibro-muscular portion of the uterus that measures 2.5 to 3.0 cm[1] lined by two types of epithelium an outer squamous epithelium and internal mucin secreting columnar epithelium, with unique junctional area containing reserve/basal cells[2]. This epithelium is vulnerable to many pathological changes ranging from inflammation to an extremely lethal malignant transformation. Due to easy accessibility to the cervix and the effective screening programme cervical cancer is reduced in the developed countries, ranking as the eighth most common cause of cancer mortality in some countries as in USA[3]. But still cervical cancer remains the most common gynaecologic malignancy in the world and the second most frequently diagnosed cancer in women worldwide after breast cancer. The majority of cases occur in developing countries[4].

A wide variety of non-neoplastic lesions occurs in the uterine cervix and is prone to varying extents of misinterpretation. The most common error is to mistake one of these benign but sometimes exuberant processes as neoplastic with potentially adverse consequences for the patient in the form of inappropriate treatment. Among women in worldwide carcinoma uterine cervix is one of the leading causes of cancer death accounts for 2% of total death in women due to cancer. In India 90,000 of new cases of cervical cancer occur every year[5,6]. The Pap smear is a screening test to detect potential gynaecological cancers .The goal of cervical cancer screening by cytology using Papanicolaou (Pap smear examination) testing is to detect and remove the precursor lesions of cervical cancer and thereby decrease the incidence of cervical cancer.[7] A serious proportion (36-70%) of the previously screened women with invasive cervical cancer are reported to have had abnormal smear findings more than 6 months prior to cancer diagnosis[8,9]. Conventional cervical cytology is the most widely used cervical cancer screening test in the world and cytology screening programmes in several developed countries have been associated with impressive reduction in cervical cancer burden[10].Squamous intraepithelial lesions are viewed as precancerous lesions exhibiting many of the morpho-logical characteristics of invasive carcinomas. Identification of these entities is the focus of cervical screening programs that aim to discover them and commence their treatment in order to prevent invasive disease. Though data from the twenty populations based cancer registries in India indicate a steady decline in cervical cancer incidence rates over the last two decades it still occupies second position and the risk of disease is still high. To detect this widely prevalent cancer at an early stage the simplest test has been a pap smear. Among the various non-neoplastic lesions cervical inflammations due to non-infective and infective causes were common. The term chronic cervicitis may indicate only the duration of the symptoms which becomes very difficult for the

gynecologist to correlate with clinical diagnosis. Other lesions such as tunnel clusters, mesonephric hyperplasia, endometriosis, and microglandular endocervical hyperplasia may be misinterpreted as malignant[11]. Thus categorization and familiarity of the cervical non-neoplastic lesions with their histopathological findings are essential in their recognition and could improve the approach toward better management of the patient. Histopathologic studies of the cervix along with clinical and cytopathological correlation are very important for early diagnosis of the cervical diseases as they have advantage of being readily available relatively cheap and technically easy[12]. Hence this study aims to study the correlation of cytological and histopathological correlation of cervical lesions.

Study design: Hospital based cross sectional study

Total cases: 1064 cases presenting with cervical lesions collected in the study period of 2 years retrospectively and prospectively.

Study place: Dept. of Pathology, S.P.Medical College, Bikaner

Study population: Patients presenting with cervical lesions.

Study Unit: cervical smear and biopsy specimens obtained from study population

Sampling method: Convenience non-probability sampling

Sample size: All patients reporting to the Pathology dept. within study duration and eligible as per inclusion criteria were included in the study.

Source of data:

The material for study will comprise of

1. Cytosmear- made from material obtained by taking smears from cervix.
2. Biopsy- from surgically removed specimen.

All the cervical smears and biopsy or surgically excised specimens and reference material submitted to the Department of Pathology, SPMC, Bikaner for histopathological study during study period.

Inclusion criteria:

1. All females with clinical presentation assosciated with cervical pathology or cervical lesions will be included in this study.

Exclusion criteria:

1. Necrotic smear and specimens.
2. Inadequate smear and biopsy.

Methods of collection of data:

Clinical data will be obtained from hospital record and requisition submitted along with cervical smear and tissue specimen received in the department. Tissue bits were routinely processed. Three to five micron thick sections will be made from paraffin blocks and was stained with H&E stain. Special stains shall be done whenever necessary. Smears and Specimen obtained from eligible study population will be examined microscopically to assess type of cervical lesion.

Data analysis: after entering data into Excel Worksheet, it was analysed with the help of frequency, proportion, mean, standard deviation and tests of significance wherever applicable.

2. Observation and Results

The present study was undertaken for cytopathological correlation of cervical lesions, in department of pathology Sardar patel Medical College, Bikaner. This study was conducted on a total 1065 cases out of which 65 cases were excluded because of unsatisfactory smear. Hence 1000 cases were taken of which both cytological and histopathological examination was done and the observations are as follows:

Table 1: Showing age distribution of Cervical lesions

Age group (Years)	Distribution of total cases	Percentage of cases
15-30	60	6.00%
31-45	267	26.70%
46-60	308	30.80%
>60	365	36.50%
Total	1000	100%

The table showing age wise distribution of study population where maximum number of patients were more than 60 years in age (36.50%), followed by 46-60 age group (30.80) and minimum number were in age group of 15-30 years (6%). mean age among cancer patient was high (51.94) with standard deviation of 12.30 and 39.53 in non cancerous patients with standard deviation of 9.66.

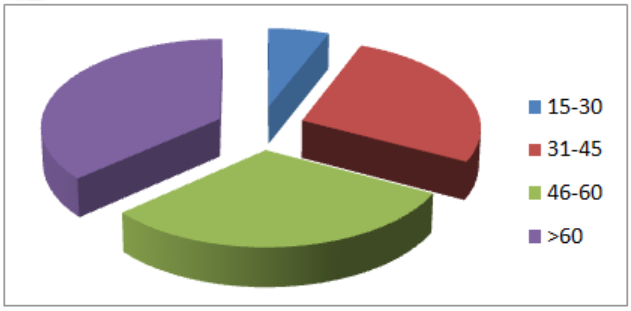

Figure 1: Showing age distribution of Cervical lesions

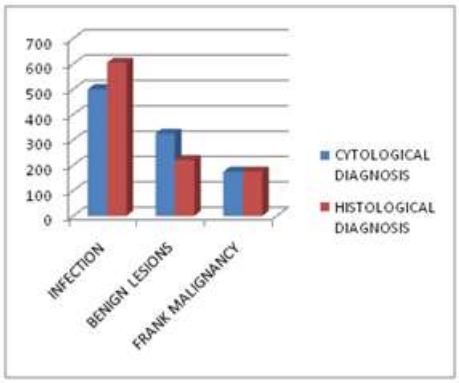

Figure 2: Comparison of cytological and histopathological findings

Table 2: Showing Mean Age

Age	Cervical Ca(No=175)		Non-malignant (Number=825)	
	Mean	SD	Mean	SD
Mean	51.94	12.30	39.53	09.66
T	14.51			
P	<0.001			
Significance	Highly Significant			

Most of the cancer cases were seen in the age group of 46-60 years. The mean age among cancer cases was high (51.94±12.30 years) and (39.53±9.66 years) in cases who did not have cervical cancer was calculated by applying t-test. Association between age group of cancerous patients and non-cancerous patients were highly significant p value<0.001).

The t-value measures the size of the difference relative to the variation in sample data, calculated difference represented in units of standard error. The greater the magnitude of T (it can be either positive or negative), the greater the evidence *against* the null hypothesis that there is no significant difference. The closer T is to 0, the more likely there isn't a significant difference**.**

p-value or probability value is the probability for a given statistical model that, when the null hypothesis is true, the statistical summary (such as the sample mean difference between two compared groups) would be the same as or of greater magnitude than the actual observed results.

Table 3: showing distribution of patients according to parity

Parity of cases in study population	No of cases	Percentage of cases
1	40	4%
2	204	20.4%
3	284	28.4%
4	212	21.2%
5	60	6%
>5	5	5%
Total	1000	100%

Table showing distribution of patients according to parity, In the present study maximum patient were multiparous and multiparity is proven risk factor for cervical malignancy with maximum number of malignancy cases reported in parity 3 (284 cases) followed by parity 4 (212 cases) and minimum cases of cervical cancer were found in parity 1 (40 cases).

Table 4: Showing duration of Symptoms

Duration of symptoms (Years)	Distribution of total number of cases	Percentage of cases
Up to 1	720	72.00%
1-3	140	14.00%
4-6	95	9.50%
>6	45	4.50%
Total	1000	100%

Table showing distribution of study population with duration of their presenting symptoms, Duration of symptoms varied from few months to many years, maximum patients presented within 1 year (72%) followed by 1-3 years (14%).

Table 5: showing the types of symptoms

Symptoms	Number of patients	Percentage of cases
vaginal discharge	580	58%
irregular vaginal bleeding	470	47%
abdominal pain	600	60%

In 1000 cases, various symptoms were seen, most of the patients showed mixture of symptoms. Majority of patients (60%) presented with abdominal pain followed by vaginal discharge (58%) followed by irregular bleeding (47%). Menstrual changes were also seen in large number of patients.

Table 6: Showing Cytological Diagnosis

Diagnosis	Distribution of cases	Percentage
Inflammatory	500	50.00%
ASCUS	135	13.50%
LSIL	80	8.00%
HSIL	110	11.00%
frank malignancy	175	17.50%
Total	1000	100%

Table showing that on cytological examination, 50% cases among study population were inflammatory smears and frank malignancy was reported in 17.5% cases, LSIL and HSIL was reported in 8% and 11% respectively.

Table 7: Showing Histopathological Diagnosis

Diagnosis	Distribution (n=1000) Number	Percentage of cases
Infections	605	60.50%
Carcinoma	175	17.50%
Dysplasia	170	17.00%
Benign Tumors	50	5.00%
Total	1000	100%

Maximum number of cases on biopsy were those of infections (60.50%), Squamous intraepithelial lesions were seen in 170 patients. Similar cases were those of frank malignancy with benign lesions comprising of only 5% in study population.

Table 8: Distribution on the basis of nature of benign lesion

Nature of lesion	Number of cases	percentage
Chronic cervicitis	570	94.21%
Chronic cervicitis with squamous metaplasia	15	2.4%
Atrophic cervicitis	20	3.3%
Total	605	100%

Table showing nature of cellular lesions in cervicitis, out of 605 inflammatory lesions maximum casese were those of chronic cervicitis (570 cases) and minimum cases were that of chronic cervicitis with squamous metaplasia(15 cases).

Table 9: Comparison of cytological and histopathological findings

Diagnosis	Cytological Diagnosis	Histological Diagnosis	P-Value
Infection	500	605	0.012%
Benign Lesions	325	220	0.001%
Frank Malignancy	175	175	0.954%

Most common diagnosis being infection 450 cases in cytology and 605 cases in histopathology, which came out to be non significant with p-value of 0.012, invasive squamous cell carcinoma (17.5%) in both cytological and histopathological findings was also found to be non-significant with the p-value of 0.954.Benign lesions accounted for 325 cases in cytology while 220 cases were diagnosed as benign in histopathology. Which were significant with a p-value of 0.001. p-value or probability value or asymptotic significance is the probability for a given statistical model that, when the null hypothesis is true, the statistical summary (such as the sample mean difference between two compared groups) would be the same as or of greater magnitude than the actual observed results.

3. Discussion

The present study was undertaken for cytopathological correlation of cervical lesions, in department of pathology Sardar Patel Medical College, Bikaner. This study was conducted on a total 1065 cases out of which 65 cases were excluded because of unsatisfactory smear. Hence 1000 cases were taken of which both cytological and histopathological examination was done.

Cancer cervix is considered to be an ideal gynaecological malignancy for screening as it meets both test and disease criteria for screening. It has a long latent phase during which it can be detected as identifiable and treatable premalignant lesions which precede the invasive disease and the benefit of conducting screening for carcinoma cervix exceeds the cost involved[51]. Despite the success of cervical cancer screening programs questions remain about the appropriate time to begin and end screening. This review explores epidemiologic and contextual data on cervical cancer screening to inform decisions about when screening should begin and end. The incidence and mortality rates from, cervical cancer that have had a Pap smear within 3 years of symptoms have decreased since 2000.

In our study distribution maximum numbers of patients were more than 60 years in age (36.50%), followed by 46-60 age group (30.80%) and minimum no. were in age group of 15-30 years (6%). Mean age among cancer patient was high (51.94%) . Vijay kumar bodal et al[12] also had the similar findings with more than half (54.50%) were aged between 31 to 45 years followed by 20.50% between 46 to 60 years. The mean age of patients with cancer in the present study was 51.24 years. This is close to that found by Biswas et al[13] and Missaoui et al[45]. Although, invasive cancer cervix is reported at all ages; it has two peaks, one at about 35 years and another above 50 years. The highest age of cervical cancer in the present study was 73 years and the lowest was 26 years. The mean age for non-cancer cases were 39.53 years. Most of patients were of group 41-50 years which were 106 (42.4%), followed by group 51-60 years which was 53 (21.2%).

In our study, the most common symptoms was discharge per vaginum (58%) followed by irregular bleeding in 47% of the patients. Patients with cancer also presented with post-coital bleeding and in cases of older age group post menopausal bleeding was seen. Symptomatic presentation was similar to some extent as seen by Ikram et al[14].

In this study, 59% patients had the cytological diagnosis of benign/ inflammatory and carcinoma was present in 10% of the cases. This is comparable to Saha and Thapa[15] in which benign cases were 51.16% and carcinoma was diagnosed in 6.97% of the cases. Most common cancer in the present study was squamous cell carcinoma (85.18%). This study showed results similar to those seen by Ikram et al[14](83.33%). As regards the various histopathological varieties of Squamous cell carcinoma, the present study found an incidence of 67.39% for moderately differentiated Squamous cell carcinoma, 23.91% for well differentiated and 8.70% for poorly differentiated. Thus, the findings of the present study are consistent with that.

Our study concluded that out of 1000 case population maximum no. of malignancy cases reported in parity 3 (28.4% cases) followed by parity 4 (21.2% cases) and minimum cases of cervical cancer were found in parity 1 (4% cases)

Which is comparable to study conducted by Rathod GB et al[17] that found out that majority of cases were of parity 3 which were 71 (28.4%) followed by of parity 4 which were 53 (21.2%), with mean parity of patient was 3.30. The study done in 2005 by Saha R, et al.[16] showed mean parity of patient 2.3 which is less as the population in this study.

For the accuracy of cytology comparing with histopathology we had calculated sensitivity (100 %) and specificity (100 %) which is comparable to study conducted by Rathod GB et[418] al who calculated their sensitivity (89.74%) and specificity (96.24%) . These

findings were comparable to the study by chabra Y, et al[19].
[10] and Kulkarni Padmaja R, et Al[20].

Table 11: Comparison of sensitivity of different studies relevant to our study

Study	Year	Sensitivity
Krishnan k et al[51]	2016	87
Chaitnya k et al[52]	2016	65
Gordana m sosic[53]	2015	67
Rathod GB,[48]	2015	8
vijay kumar Bodal et al[43]	2014	89
Smitha et al[54]	2014	94
M. suguna et al[55]	2014	95
Ragheshwar jyotI et al[56]	2013	78.6
Kyoung bun lee et al[57]	2009	66.5
Miheala muntean et al[58]	2010	58.8
Pradhan b et al[59]	2007	65.5
Krislma algotar et al[60]	2004	73
GPS Yeoh et al[61]	1997	55
Bruce A. Jones et al[62]	1996	89.4
W.F. kealy et al[63]	1986	87

In our study conducted on study population of 1000 cases during the study period we founded the pattern of cervical lesions as infections in 60.50%cases, carcinoma in17% cases ,dysplasia in17% of cases , benign tumors in only 5% cases which is comparable to Chaitnya k et al[52] who conducted a study on a total number of 5559 smears and included inflammatory changes 4413 (79.38%), normal 983 (17.68%), precancerous and malignant 123 (2.2%),low-grade squamous intraepithelial lesion , 20 (16.2%), squamous cell carcinoma 16 (13%), and adenocarcinoma 1 (0.8%). Gordana M Sosic et al[53] also found out that maximum number of cases belonged to infection 65% and carcinoma 10.8%. and dysplasia accounting for 18% which is comparable to our study as well as with vijay kumar bodal et al[43],Krislma algotar et al[60]. Which is shown in tabulated manner below.

Table 12: Showing frequency distribution of various cervical lesions histologically

Sr no.	Authors	Krishnan K,[51]	Chaithanya K[52]	Gordana m sosic[53]	vijay kumar Bodal et al[43]	Smitha krishnegonda et al[54]	Krislma algotar[60]	Present study
1	Total number of lesion	78	5559	120	200	432	70	1000
2	Infections	62%	74.33%	65%	59%	58%	45%	60.50%
3	Carcinoma	14	2.21%	10.9%	10%	20%	31%	17.50%
4	Dysplasia	16	11.46%	18%	20%	12%	9%	17.00%
5	Benign Tumors	8	12%	6.1%	11%	2%	20%	5.00%

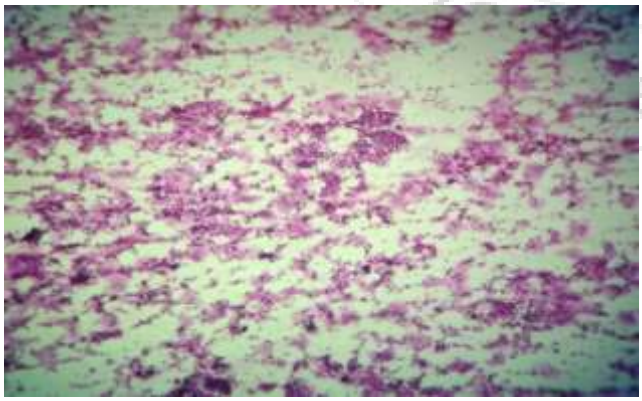

Figure 1: Scanner view (4X) of cytological image of chronic non specific inflammation on H&E stain

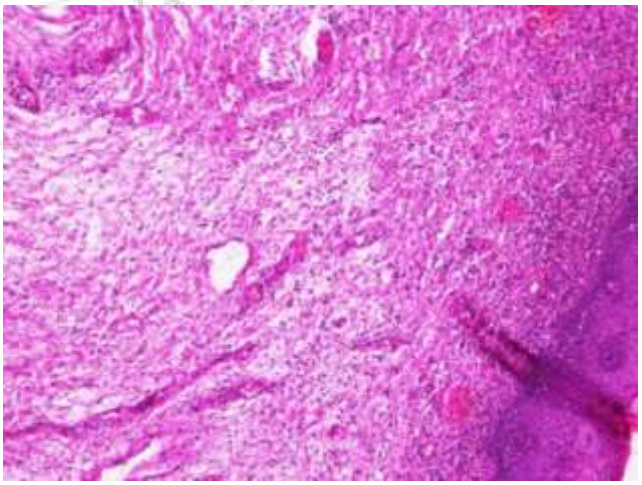

Figure 2: Scanner view of histological image of chronic non specific cervicitis on H&E stain

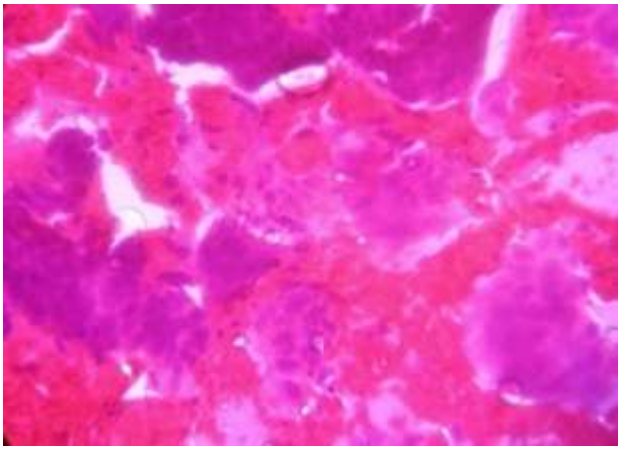

Figure 3: Scanner view of low grade squamous intraepithelial neoplasia on H&E stain

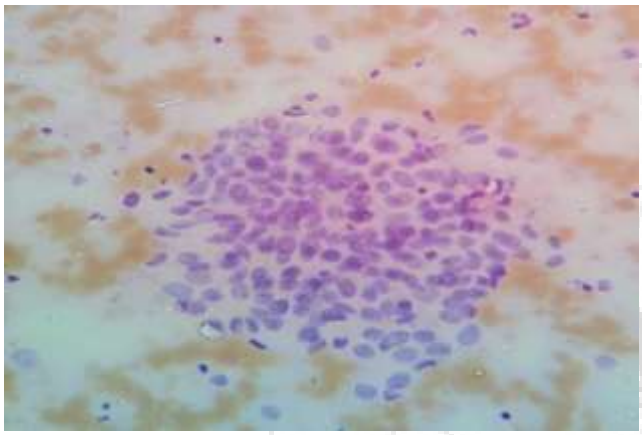

Figure 4: Scanner view of high grade squamous intraepithelial neoplasia on H&E stain

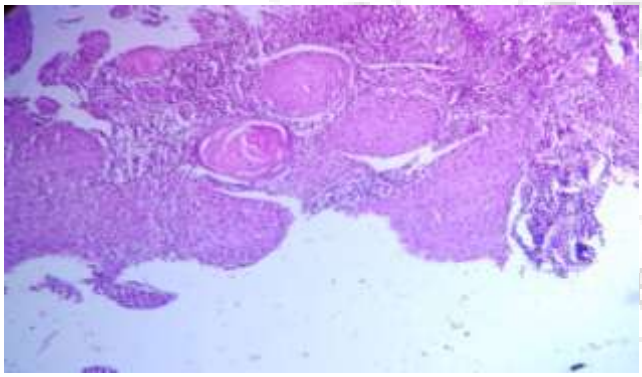

Figure 5: scanner view of well differentiated squamous cell carcinoma in histology

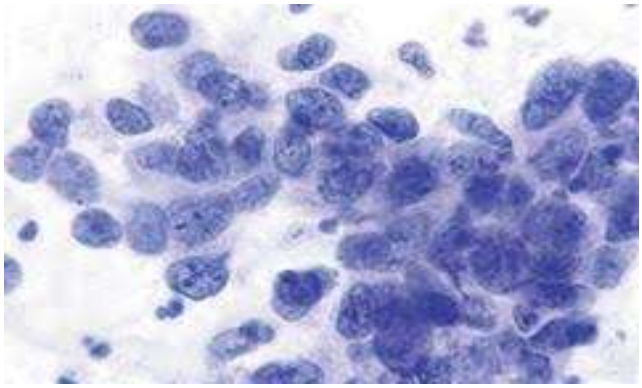

Figure 6: High power view (40X) of squamous cell carcinoma in cytology

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