MAK HILL Publications Research Journal of Medical Science

Research Article
doi: 10.59218\makrjms.2023.103.109

The Diagnostic Utility of PAP Smear Cytology and Histopathological Correlation in the Cases of Cervical Carcinoma and Precancerous Cervical Lesion at Tertiary Center

[1]Mital Kundariya, [2]Meghavi Joshi, [1]Kosha Panchal and [3]Nikhil Anand

[1]Ex Resident Gujarat Cancer Research Institute, Ahmedabad, Rajkot, Gujarat, India

[2]Department of Pathology, Institute of Nootan Medical College and Research, Visnagar, Gujarat, India

[3]Department of Obstetrics and Gynecology, GMERS Medical College, Vadnagar, Gujarat, India

ABSTRACT

Cervical carcinoma is one of the common cancer in indian female population. The cervical epithelial cells can exfoliate and a prolonged natural history of the pre-cancerous lesions is very helpful for the diagnosis of cervical carcinoma and pre-cancerous lesion. PAP smear is the very effective test to prevent and detect pre-cancerous lesion of the cervix before they become invasive cancer, However, false negative results may present due to sampling error or interpretation error. The confirmatory diagnosis should be made on histopathological examination and correlated for assessing the accuracy of the PAP smear cytology. (1) To study the importance of cytological (PAP smear) examination in cervical carcinoma and pre-cancerous lesio and (2) To study the histopathologcal correlation and Imunohistochemistry in cervical carcinoma and pre-cancerous lesion. Study of cases of cervical carcinoma and pre-cancerous lesion in which both PAP smear and histopathology samples were received during the period of 3 years. A detailed clinical history obtained from case files and records. The conventional PAP techniques using PAP stain, To eliminate subsampling and to obtain monodispersion of cells and clear background we used a newer technique-liquid based cytology by sure path method. Tissue samples were fixed, processed and stained with hematoxylin and eosin. In cases where needed further immunohistochemical markers were studied. Total 102 Cervical PAP test were examined and correlated with histopathological findings. In this study most of patients were of age group 40-59 year. Among the 102 cases, 66 (64.7%) patients were of postmenopausal age and there were 12, 8, 6, 23, 2 and 7 cases of ASCUS, ASC-H, LSILs, HSILs, AGC, AGUS, respectively. About 41 patients diagnosed as squamous cell carcinoma and 3 patients as adenocarcinoma. The histopathological examination of the specimen represented as follows: 6.86% CIN1, 1.96% CIN 2, 13.72% CIN3, 61.76% squamous cell carcinoma, 7.84% Adenocarcinoma and 7.84% were given false positive. Most of patients with cervical carcinoma and pre-cancerous lesions were in postmenopausal age. Multiparity is risk factor for cervical carcinoma. Squamous cell carcinoma of cervix was most common malignant lesion of cervix. PAP smear is an effective screening method for early diagnosis of pre-cancerous lesions and carcinoma of cervix so better awareness and motivation programs are recommended for prevention of cervical cancer. However, cervical biopsy is gold standard for accurate diagnosis and confirmation of cervical malignant lesions.

OPEN ACCESS

Key Words
Squamous cell carcinoma, PAP smear, Immunohistochemistry

Corresponding Author
Nikhil Anand
Department of Obstetrics and Gynecology, GMERS Medical College, Vadnagar, Gujarat, India
Tel: 9227499196

Received: 2 March 2023
Accepted: 25 May 2023
Published: 15 June 2023

Citation: Mital Kundariya, Meghavi Joshi, Kosha Panchal and Nikhil Anand 2023. The diagnostic utility of PAP Smear Cytology and Histopathological Correlation in the Cases of Cervical Carcinoma and Precancerous Cervical Lesion at Tertiary Center. Res. J. Med. Sci., 17: 103-109, doi: 10.59218\makrjms.2023.103.109

INTRODUCTION

Cancer of uterine cervix is the commonest cancer in female in developing countries like India[1]. The cervical epithelial cells can exfoliate along with prolonged history of the pre-cancerous lesions is very helpful for the diagnosis of cervical carcinoma and pre-cancerous lesion. PAP smear is the very effective test to prevent and detect pre-cancerous lesion of the cervix before they become invasive cancer, However, false negative results may present due to sampling error or interpretation error. The final diagnosis should be made on histopathological examination to assess the accuracy of the PAP smear cytology. This study has been carried out to correlate the cytological and histopathological findings of the cervical carcinoma and pre-cancerous lesion. Study will also focus to evaluate importance of Immunohistochemistry in these cases.

Aims and objectives:

- To study the importance of cytological (PAP smear) examination incervical carcinoma and pre-cancerous lesion
- To study the histopathologcal correlation and Imunohistochemistry in cervical carcinoma and pre-cancerous lesion

MATERIALS AND METHODS

This is a study of cases of cervical carcinoma and pre-cancerous lesions visited the hospital during the period of 3 year. Only those newcases in which both cytological and histological samples were received are included in the study. A detailed clinical history regarding Findings of per-speculum examination and per-vaginal examination were taken into consideration. In this study samples for PAP smear were collected from endocervical canal squamo-columnar junction and Stained by conventional PAP techniques using PAP stain. Major drawback of conventional PAP smear technique is inadequate sampling. To eliminate subsampling and to obtain monodispersion of cells ANDclear background we used a newer technique-liquid based cytology by sure path method. Histopathological samples include cervical biopsy or endocervical curettage (ECC) material was processed and stained by hematoxylin and eosin. In cases where needed further immunohistochemical markers were studied.

RESULTS

In this study correlation of cytological features with histopathological findings in cervical carcinoma and pre-cancerous lesion were evaluated. Total 102 PAP smears were examined and correlated with

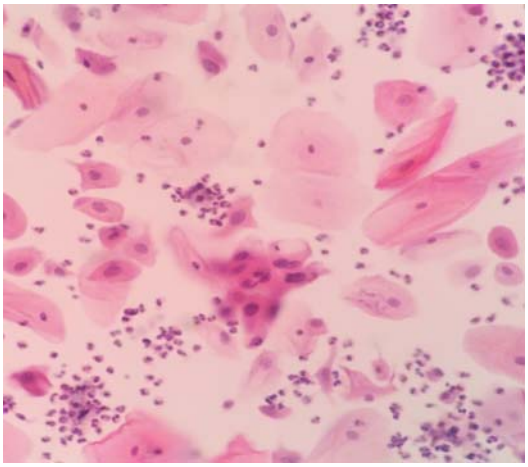

Fig. 1: Atypical squamous cells-undetermined significance (LBC, 40X)

Table 1: Age range of the patients

Age range	No. of patients	Percentage
20-39	10	9.80
40-59	59	57.84
60-79	32	31.38
80-99	1	0.98
Total	102	100.00

Table 2: History of parity of the patients

History of parity	No. of patients	Percentage
0-2	35	34.31
3-5	63	61.76
6-7	04	3.92
>7	00	0.00
Total	102	100.00

Table 3: Menstrual history of patients

Menstrual history	No. of patients
Menopause	66 (64.70%)
Irregular menstrual bleeding	15 (14.70%)
Regular menstrual bleeding	21 (20.58%)
Total	102 (100%)

histopathological findings. In our study most of patients presented in age range of 40-59 years (Table 1 and 2). About 66 (64.7%) patients were in postmenopausal age group (Table 3-6).

The presence of atypical epithelial cells examined and interpretated according to Bethesda classification. The ASCUS showing increased nuclear size, mild nuclear hyperchromasia with regular nuclear shape (Fig. 1). ASCH-enlarge nucleus than those of metaplastic cell or intermediate cells, hyperchromasia and irregular nuclear membranes (Fig. 2).

LSIL-larger cells with high n:c ratio, hyperchromasia, bi and multinucleated, absent or inconspicuous nucleoli andmature cytoplasm (Fig. 3). HSIL-atypical epithelial cells arranged singaly or in clusters and sheets showing marked pleomorphism, dark nuclei, high N: C ratio, granular nuclear chromatin, irregular nuclear membrane with indentations, with variable cytoplasm (Fig. 4).

Squamous cell carcinoma showing highly cellular smears and malignant epithelial cells arranged in clusters or singaly scattered. Tumor cells having

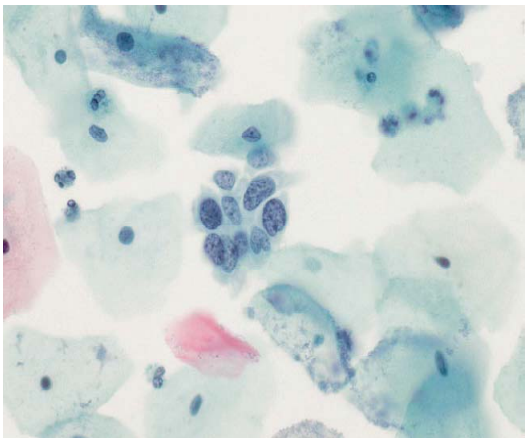

Fig. 2: Atypical squamous cells-cannot exclude an HSIL (LBC, 40X)

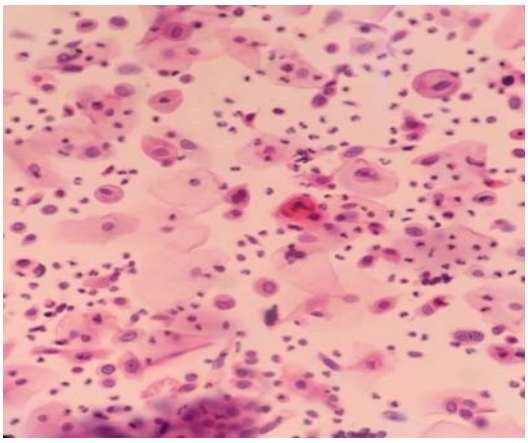

Fig. 4: High-grade squamous intraepithelial lesion-(LBC, 40X)

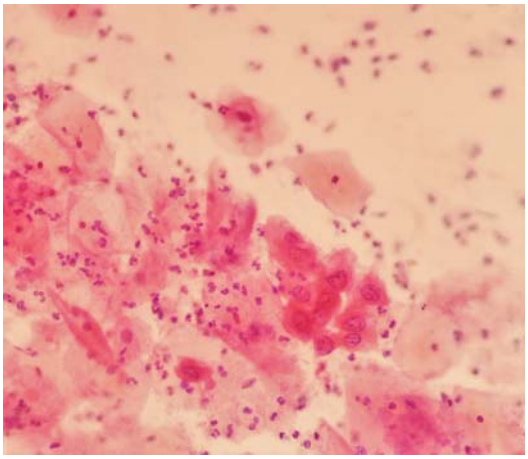

Fig. 3: Low grade squamous intraepithelial lesion (conventional PAP, 40x)

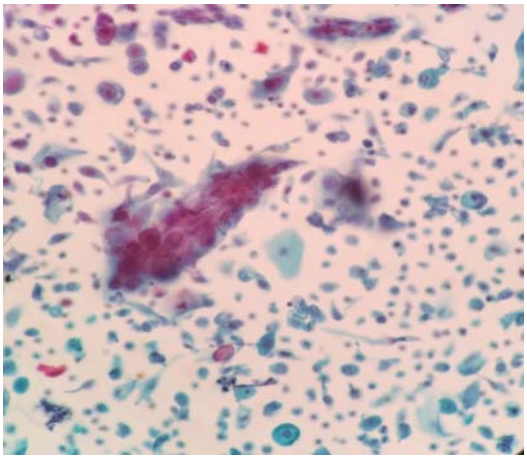

Fig. 5: Squamous cell carcinoma (LBC, 40X)

Table 4: Symptoms of patient presented

Symptoms of patients	No. of patients	Percentage
Asymptomatic	23	22.54
Discharge per vagina	39	38.23
Post-menopausal bleeding	32	31.37
Post coital bleeding	09	8.82
Irregular-menstrual bleeding	06	5.88

Table 5: Cases distribution of cervical carcinoma and pre-cancerous lesion

Category	No. of cases	Percentage
Malignant	71	69.60
Premalignant	23	22.54
Negative	8	0.07
Total	102	100.00

Table 6: Per speculum examination of patient

P/S Findings	No of patients	Percentage
Normal	29	28.43
Erosion	15	14.70
Cervicitis	15	14.70
Polyp	05	4.90
Suspicious for malignancy	34	33.33
Frank malignant growth	04	3.92

irregular, hyperchromatic nuclei with moderate or abundant cytoplasm and evidence of necrotic material in background (Fig. 5).

AGC-smear show glandular cells with crowding, nuclear overlapping, 3-4 times increased in size of nucleus with nuclear hyperchromasia (Fig. 6). The AGUS smear show sheets of cells with crowding and overlapping of nuclei, high N:C ratio and hyperchromasia (Fig. 7).

Adenocarcinoma presented with clusters and syncytial clusters of cells with large irregular nucleus, irregular nuclear chromatin, macronucleoli and fine vacuolated cytoplasm and tumor necrosis present in all cases (Fig. 8).

Low grade squamous intra epithelial lesion shows basal and parabasal hyperplasia involving to lower 1/3 of epithelium and upper layer exhibits koilocytic changes on histological section (Fig. 9). High grade squamous intra epithelial lesion on histological section show full thickness immaturity, irregular polarity and abnormal mitotic figures (Fig. 10 and 11). Squamous cell carcinoma on histological section shows sheets and nests of infiltrative tumor cells with desmoplastic

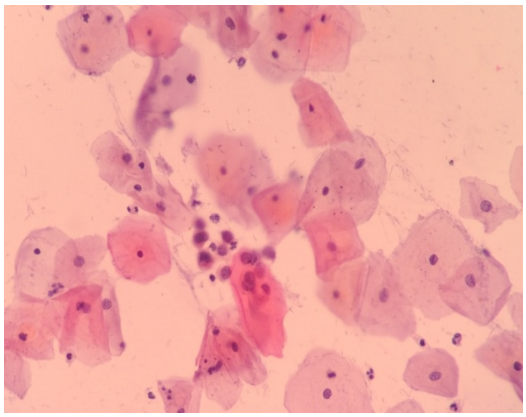

Fig. 6: Atypical glandular cell (LBC, 40X)

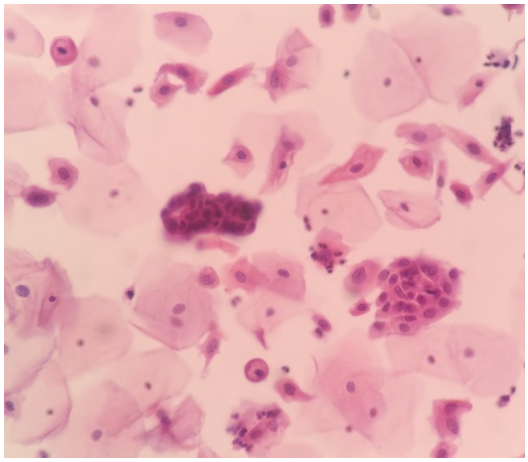

Fig. 7: Atypical glandular cell-undetermined significance (LBC, 40X)

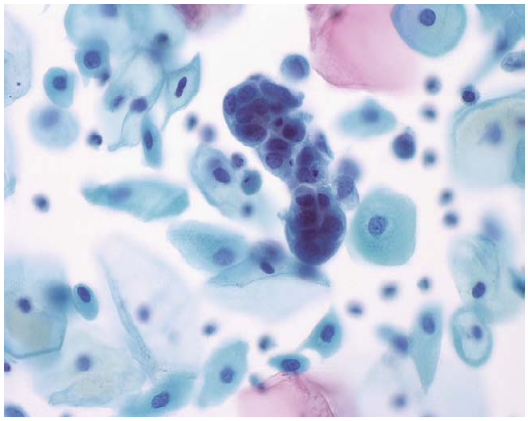

Fig. 8: Adenocarcinoma (LBC, 40X)

stromal reaction (Fig. 12). Adenocarcinoma shows large, confluent, cribriform glands with psedostratification and necrotic debris in glands (Fig. 13).

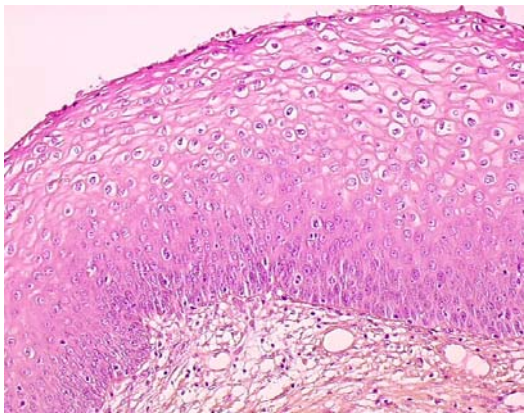

Fig. 9: Cervical intraepithelial neoplasm I-(H and E, 40X)

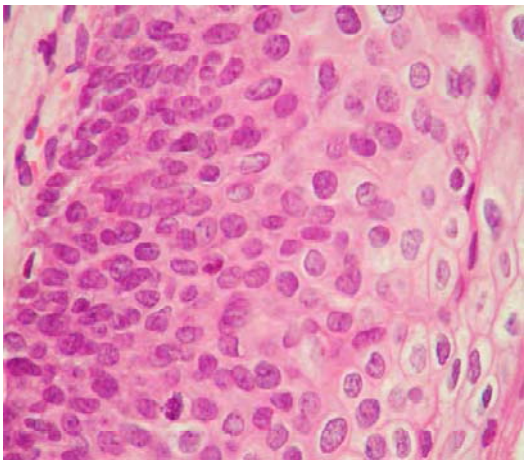

Fig. 10: Cervical intraepithelial neoplasm II-H and E, 40X)

Table 7: PAP smaer interpretation by Bethesda system (2014)

Interpritation	No. of cases	Percentage
ASCUS	12	11.76
ASC-H	08	07.84
LSIL	06	05.88
HSIL	23	22.54
AGC	02	01.96
AGUS	07	06.86
SCC	41	40.19
Adenocarcinoma	03	02.94
Total	102	100.00

Out of the 102 cases of cervical carcinoma and pre-cancerous lesions, there were 12 (11.76%), 8 (7.84%), 06 (5.88%), 23 (22.54%), 2 (1.96%) and 7 (6.86%) cases of ASCUS, ASC-H, LSIL, HSIL, AGS and AGUS, respectively. 41 (40.19%) had squamous cell carcinoma (SCC) and 3 (2.94%) adenocarcinoma (Table 7).

Corresponding histopathology of the tissue specimen were represented as follows: 6.86% CIN1, 1.96% CIN 2, 13.72% CIN3, 61.76% Squamous cell carcinoma, 7.84% Adenocarcinoma and 7.84% were given false positive (Table 8).

Table 8: Correlation between cytological and histological diagnosis

	Cytological diagnosis								
Histology diagnosis	ASCUS	ASC-H	LSIL	HSIL	SCC	AGC	AGUS	ADENO	Total
Negative/non malignant	4			1			3		8
CINI	3		4						7
CINII				1			1		2
CINIII		4		9	1				14
SCC	5	4	2	12	40				63
Adenocarcinoma						2	3	3	8
Total	12	8	6	23	41	2	7	3	102

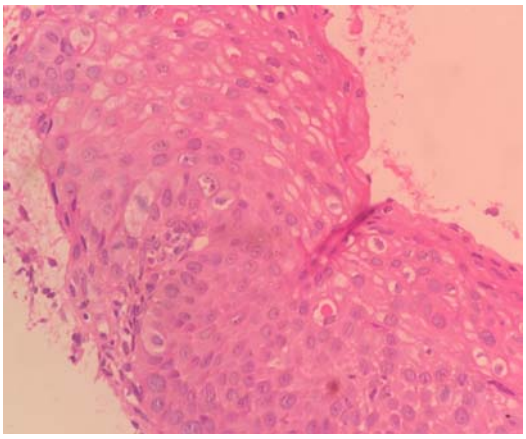

Fig. 11: Cervical intraepithelial neoplasm III: (H and E, 40X)

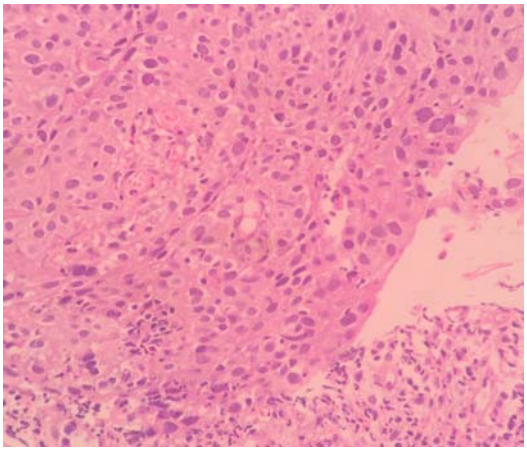

Fig. 12: Squamous cell carcinoma (H and E, 20x)

DISCUSSIONS

In this study, 102 cases of cervical carcinoma and pre-cancerous lesions of uterine cervix presenting at tertiary hospital of Gujarat were studied with detailed clinical history, cytological and histomorphological findings. The precancerous conditions known as Dysplasia or Cervical Intraepithelial Neoplasia and that can be detected early by PAP smear cytology. It takes many years for precancerous lesion to transform into malignancy so easy diagnosis and treatment can prevent the cervical carcinoma.

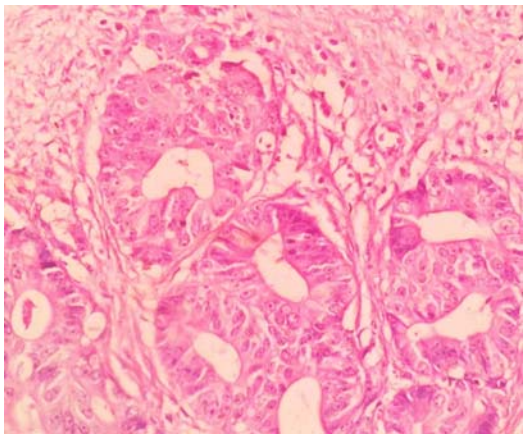

Fig. 13: Adenocarcinoma: (H and E, 40X)

The majority of our patients were in the age of 40-59 years which are similar to other studies have observed in which women with more than 40 years of age as in Srivastava *et al*.[2] and Kalyani *et al*.[3]. The age group involved in carcinoma cervix ranged from 35-50 years in Aswathy *et al*.[4].

Out of the 102 cases, 66 (64.7%) patients were of postmenopausal (40-59) age group. That is comparable 60.7% with study Bukhari *et al*.[5].

In our study multiparity is the one of the risk factor of malignancy which is comparable with multiparous woman has increased risk of malignancy in the study of Gundrajakuppam *et al*.[6] women with 3 or more births showed increased risk of carcinoma cervix in the study of de González *et al*.[7]

Abnormal vaginal discharge and bleeding was the commonest presentation in patients of malignancy which is also in the study of Gundrajakuppam *et al*.[6].

Out of 102 cases, 71 (69.60%) cases are malignant and 23 (22.54%) cases are pre-malignant. Majority of cases were malignant constituting 69.60%.because our study was done at tertiary referral centre. About 40.0% cases diagnosed as squamous cell carcinoma on both cytology and histology so the concordance rate is 63.49% for squamous cell carcinoma. Out of 23 discordant cases, 12 cases diagnosed as HSIL, 4 cases as LSIL, 5 cases as ASCUS and 4 cases as ASC-H. Main factor in under reporting was inadequate sample collection, less cellularity with haemorrhagic background, air drying and fixation artifacts (Table 9).

Table 9: Cytological and histological examination in squamous cell carcinoma with the concordance rate in other studies

Studies	Cases	Concordance rate (%)
Saha and Thapa[8]	3/3	100.00
Yeoh and Chan[9]	6/11	54.50
Nawaz *et al*.[10]	73/75	97.30
Jain and Vyas[11]	163/195	83.60
Present study	40/63	63.49

Table 10: The concordance rate between cytological and histological examination for Cervical Intra epithelial Neoplasia II and III in various studies

Studies	Cases	Concordance rate (%)
Saha and Thapa[8]	72/102	70.59
Yeoh and Chan[9]	72/128	55.56
Nawaz *et al*.[10]	22/40	55.00
Jain and Vyas[11]	6/31	26.08
Present study	10/16	62.50

Table 11: Comparison of concordance rate between cytological and histological examination for Cervical Intraepithelial Neoplasia I with various studies

Studies	Cases	Concordance rate (%)
Saha and Thapa[8]	6/8	75.00%
Yeoh and Chan[9]	37/86	50.70%
Nawaz *et al*.[10]	28/56	50.00%
Jain and Vyas[11]	9/14	64.30%
Present study	4/7	57.14%

Total 16 cases of CIN II and III, 10 cases diagnosed in cytology and the concordance rate is 62.50%. Six cases were discordant out of which 4 cases diagnosed as ASC-H on cytology and one case diagnosed squamous cell carcinoma the main cause for discrepancy being interpretation error (Table 10).

The concordance rate for CIN I in present study is 64.3% as compared to Saha's study having the rate of 75%, In the study of Yeoh and Thapa[8] study having 50.68%, Nawaz study gives the concordance rate of 50% and Jain V study shows 64.30% concordance rate. All three discordant cases were diagnosed as ASCUS. However, out of three cases in two cases there was presence of obscuring inflammation (Table 11).

Squamous cell carcinoma is the most common type of cervical cancers. In our study out of malignant cases, 88.73% (63/71) were squamous cell carcinoma and 11.26% (8/71) were adenocarcinoma. Various Studies have also shown that 85-90% of cervical carcinoma are squamous cell carcinoma in Das *et al*.[12], Srivastava *et al*.[2] and Kalyani *et al*.[3]. Adenocarcinoma of the uterine cervix arises from the endocervical epithelial cells and about 14% of cervical carcinomas are adenocarcinoma as in Dikshit *et al*.[13].

When the histopathological diagnosis was used as a gold standard, the accuracy rate of the cytologic diagnosis within the first grade was 80.28%, which implied that 57 cases of 71 revealed matched results between cytology and histology. The 57 matched cases were comprised of 4 LSIL cases with CIN 1 in histology, 10 HSIL cases with CIN 2, CIN 3 and CIS in histology and 40 Squamous Cell Carcinoma cases and 3 adenocarcinoma cases in both cytology and histology. All ASC cases were excluded.

Seven cases of cervical biopsies were reported as adenocarcinoma of cervix. In a single case patient has suspicious mass in the lower uterine segment and cervix. Hence, IHC was applied to confirm the diagnosis as endocervical type or endometrial carcinoma spreading to cervix. CEA and Vimentin markers helped in confirm diagnosis. On IHC examination CEA positivity and Vimentin negativity favoured the endocervical carcinoma while in endometrial carcinoma CEA is negative and Vimentin is positive. In this way, IHC plays a crucial role in cases with diagnostic dilemma helping to differentiate endometrial carcinoma from endocervical carcinoma[14]. This in turn very helpful in treatment of the patient.

CONCLUSION

Majority of patients with cervical carcinoma and precancerous lesions are presented in the age group of 40-59 years and in postmenopausal age. Multiparity is risk factor for cervical carcinoma. Abnormal vaginal discharge and bleeding per vagina was the commonest presentation of patients with precancerous lesion and cervical carcinoma. Squamous cell carcinoma was most common malignant lesion of cervix. PAP smear is effective method for early diagnosis of precancerous cervical lesions and secondary prevention of carcinoma cervix. It is still a simple test with satisfactory results for diagnosis associated with cervical cancer and precancerous lesions. The good screening for cervical cancer by PAP smear is based on collection of adequate materials and correct interpretation of abnormal cells. Therefore, motivation and awareness in females are required. The liquid based cytology technique are much accurate by reducing sampling errors, technical errors. HPV, DNA testing are recommended along with cytology of PAP smear for prevention of cervical cancer. However cervical biopsy is gold standard for accurate diagnosis and confirmation of cervical malignant lesions.

REFERENCES

1. Nandakumar, A., T. Ramnath and M. Chaturvedi, 2009. The magnitude of cancer cervix in India. Indian J. Med. Res., 130: 219-221.
2. Srivastava, A., J. Misra, S. Srivastava and U. Singh, 2009. Risk-factors and strategies for control of carcinoma cervix in India: Hospital based cytological screening experience of 35 years. Indian J. Cancer, 46: 155-159.
3. Kalyani, R., S. Das, M.B. Singh and H. Kumar, 2010. Cancer profile in the department of pathology of Sri Devaraj urs medical college, Kolar: A ten years study. Indian J. Cancer, 47: 160-165.

4. Aswathy, S., M.A. Quereshi, B. Kurian and K. Leelamoni, 2012. Cervical cancer screening: Current knowledge and practice among women in a rural population of Kerala, India Indian J. Med. Res., 136: 205-120.
5. Bukhari, M., K. Saba, S. Qamar, M. Majeed, S. Niazi and S. Naeem, 2012. Clinicopathological importance of papanicolaou smears for the diagnosis of premalignant and malignant lesions of the cervix. J. Cytol., 29: 20-25.
6. Gundrajakuppam, L, V. Shanthi and N.M. Rao, 2011. Clinic pathological correlation of cervical carcinoma by PAP smear. J. Biosci. Tech., 2: 439-445.
7. de González, A.B., S. Sweetland and J. Green, 2004. Comparison of risk factors for squamous cell and adenocarcinomas of the cervix: A meta-analysis. Br. J. Cancer, 90: 1787-1791.
8. Saha, R. and M. Thapa, 2005. Correlation of cervical cytology with cervical histology. Kathmandu Univ. Med. J., 3: 222-224.
9. Yeoh, G.P.S. and K.W. Chan, 1997. The accuracy of Papanicolaou smear predictions: Cytohistological correlation of 283 cases. Hong Kong Med. J., 3: 373-376.
10. Nawaz, F.H., A.B. Aziz, S. Pervez and J.H. Rizvi, 2005. Prevalence of abnormal papanicolaou smears and cytohistological correlation: A study from aga Khan university hospital, Pakistan. Asia-Pac. J. Clin. Oncol., 1: 128-132.
11. Jain, V. and A.S. Vyas, 2010. Cervical neoplasia-cyto-histological correlation (Bethesda system) a study of 276 cases. J. Cytol. Histol., Vol. 1.
12. Das, B.C., V. Gopalkrishna, S. Hedau and S. Katiyar, 2000. Cancer of the uterine cervix and human papillomavirus infection. Curr. Sci., 78: 52-63.
13. Dikshit, R., P.C. Gupta, C. Ramasundarahettige, V. Gajalakshmi and L. Aleksandrowicz *et al*., 2012. Cancer mortality in India: A nationally representative survey. Lancet, 379: 1807-1816.
14. McCluggage, W.G., 2007. Immunohistochemistry as a diagnostic aid in cervical pathology. Pathology, 39: 97-111.