

Evaluation of pap smears with cyto-histopathological correlation—our experience at a tertiary care hospital in Telangana



Meghna Maria Tharakan¹, Sandhya Bangaru², Mark Edward M³, Smita Reddy A⁴, Anunayi Jeshtadi⁵, Harika Kalangi⁶, Danda Samyukta Reddy⁷

¹Senior Resident, ^{2,3}Assistant Professor, ⁴Associate Professor, ⁵Professor and Head, Department of Pathology, Government Medical College, Suryapet, ⁷Junior Resident, Kamineni Academy of Medical Sciences and Research Centre, Hyderabad, Telangana, India, ⁶Resident Fellow, Department of Internal Medicine, The Mount Sinai Hospital, New York, United States

Submission: 15-02-2024

Revision: 29-03-2024

Publication: 01-05-2024

ABSTRACT

Background: The World Health Organization states that cervical carcinoma is the fourth most common cancer among women worldwide. Pap smear is the simplest and easiest test to detect this prevalent cancer at its nascent stages. **Aims and Objectives:** This study aims to evaluate Pap smears using the conventional method (Bethesda 2014) and correlate the abnormal smears with cervical biopsy. **Materials and Methods:** The study is a combined retrospective and prospective study, from January 2021 to August 2023. Pap smears received were evaluated according to Bethesda 2014. Those cases categorized as Epithelial Cell Abnormality (ECA), were correlated with corresponding histopathology on cervical biopsy. **Results:** Out of the 615 pap smears in this study, 525 cases (91%) were categorized as Negative for Intraepithelial Lesion or Malignancy, 53 cases (9%) as Epithelial Cell Abnormality, and 37 cases (6%) as unsatisfactory. In the Negative for Intraepithelial Lesion or Malignancy category, 353 cases (67.2%) were reactive cellular changes including inflammation, four cases (0.7%) were squamous metaplasia, and 24 cases (4.6%) were atrophic smears. In the ECA category—21 cases (39.6%) were Atypical squamous cells of undetermined significance, two cases (3.8%) were Low-grade squamous intraepithelial lesion, five cases (9.4%) were Atypical squamous cells-cannot exclude HSIL(ASC-H), 14 cases (26.4%) were High grade squamous intraepithelial lesion (HSIL) and 3 cases (5.6%) were squamous cell carcinoma (SCC) cervix, seven cases were of ECA-glandular type (13.2%). On histopathological correlation, the maximum correlation was found for HSIL and SCC cases, 71% and 100%, respectively. **Conclusion:** Pap smear is a crucial screening tool to diagnose cervical carcinoma at its nascent stage. This study showed a positive correlation for high-grade lesions on Pap smears.

Key words: Pap; Histopathological correlation; Cervical carcinoma; Epithelial cell abnormalities

INTRODUCTION

Cervical carcinoma is one of the leading causes of death among women worldwide. The incidence is on the rise, especially in developing countries like India. It is ranked as the second most popular cancer in women in the world.¹ India contributes to more than one-fifth of cervical cancer deaths.² Early diagnosis and treatment of cervical cancer can cause a significant reduction in morbidity and mortality.

One of the easiest ways to diagnose this disease at a nascent stage is by Pap smears. Pap smear is a simple yet effective screening test to diagnose inflammatory, precancerous, and cancerous lesions of the cervix. It is a safe and simple procedure which can help assess both the ectocervix and endocervix. The human papillomavirus rates are the highest in sexually active women <25 years.³ Routine cervical screening must be followed by profound efforts to keep the patients all through the screening process, to avoid attrition

Access this article online

Website:

<http://nepjol.info/index.php/AJMS>

DOI: 10.3126/ajms.v15i5.62776

E-ISSN: 2091-0576

P-ISSN: 2467-9100

Copyright (c) 2024 Asian Journal of Medical Sciences



This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

Address for Correspondence:

Dr. Mark Edward M, Assistant Professor, Department of Pathology, Government Medical College, Suryapet, Telangana, India.
Mobile: +91-9703773232. **E-mail:** drmarkedward.m@gmail.com

during follow-up visits.⁴ Evaluation of Pap smears is done by the Bethesda system which was developed in 1988.⁵ It assesses the adequacy and classifies lesions based on a two-tier system, that is, low-grade squamous intraepithelial lesion (LSIL) and high-grade squamous intraepithelial lesion (HSIL).⁶

Aims and objectives

This study aims to evaluate Pap smears based on the Bethesda system of reporting cervical cytology 2014 and to correlate them with histopathology on cervical biopsies. The objectives are to assess and categorize the Pap smears according to the Bethesda system 2014 and to correlate the Pap smears in the Epithelial Cell Abnormality (ECA) category with histopathology on cervical biopsies

MATERIALS AND METHODS

This study is a combined retrospective and prospective study, conducted in Government General Hospital, Suryapet for a period of 2 years 8 months from January 2021 to August 2023. A total of 615 Pap smears were evaluated. The pap smears were collected in the gynecology department using a conventional technique of collection.

Inclusion criteria

The following criteria were included in the study: Women between 21 and 80 years of age, presenting with symptoms such as white discharge per vaginum, post-menopausal bleeding, irregular menstrual history, utero-vaginal prolapse, and post-coital bleeding

- Symptomatic women with normal per speculum findings
- Women with cervical findings such as erosion, hypertrophy, and cervical polyps.

Exclusion criteria

The following criteria were excluded from the study:

- Pregnant women
- Women previously treated for carcinoma cervix
- Women with previous cervical surgery
- The cervical smears were immediately fixed in 95% ethyl alcohol, stained by conventional Papanicolaou stain, and assessed in the Department of Pathology.

Conventional cytology was used to prepare the smears owing to the low resource set-up and the low cost.⁷ They were evaluated based on The Bethesda System for Reporting Cervical Cytology 2014 edition.⁵ Histopathological correlation was advised for all ECA cases and those that were clinically suspicious. The corresponding abnormal cervical biopsies were correlated.

Statistical analysis

Descriptive analysis of the data was performed using Microsoft Excel. The results are expressed in numerical values and percentages.

Ethical considerations

This study was approved by the Institutional Ethics Committee, Government Medical College, Suryapet, Telangana.

RESULTS

All the 615 Pap smears in this study were of conventional cytology. The average age of presentation was 45 years. The most common complaint at the time of evaluation was white discharge. Cervical erosion was the most common per speculum finding.

Pap smear findings

Of the 615 cases, 578 cases (94%) were satisfactory smears and 37 cases (6%) were unsatisfactory. Twenty-seven smears (73%) were unsatisfactory due to scanty cellularity and 10 smears (27%) were unsatisfactory as they were obscured by hemorrhage. Five hundred and twenty-five smears (91%) were categorized as Negative for Intraepithelial Lesion or Malignancy and 53 cases (9%) were of ECA category.

Of the 525 Negative for Intraepithelial Lesion or Malignancy, 353 cases (67.2%) were reactive cellular changes associated with inflammation (including typical repair), 130 cases (24.7%) were normal study, 24 cases (4.6%) were atrophic smears, 14 cases (2.67%) showed keratotic changes, and four cases (0.76%) showed squamous metaplasia. Of the 53 ECA cases, 45 cases (85%) were of squamous cells and seven cases (13.2%) were of glandular cells and one case (1.8%) was of Other Malignant Neoplasm category (Table 1).

Of the 45 squamous cell cases, 21 cases (46.7%) were Atypical squamous cell of undetermined significance (ASCUS) (Figure 1), 14 cases (31.1%) were HSIL (Figure 2), five cases (11.1%) were Atypical Squamous cells, cannot exclude HSIL (ASC-H), three cases (6.7%) were squamous Cell Carcinoma (SCC) (Figure 3), and two cases (4.4%) were LSIL. Of the 7 glandular cell cases, six cases (85.7%) were Atypical glandular cells (AGCs) not otherwise specified (NOS) (Figure 4) and one case (14.3%) was of Atypical endocervical cells (NOS) (Table 1).

Histopathological correlation

Fifty-four cervical biopsies were done. Of the 21 ASCUS cases, on histopathology, 12 cases were chronic cervicitis, five cases were cervical intraepithelial neoplasia-I and four cases were ectocervical hyperplasia. Of the 14 HSIL

Table 1: Percentage of cases in each category in this study			
S. No	Category	Total number of cases	Percentage
1.	Unsatisfactory	37	6.01
2.	NILM	525	85.36
2.A	Reactive cellular changes associated with inflammation (including typical repair)	353	57.4
2.B	Squamous metaplasia	4	0.65
2.C	Atrophy	24	3.9
2.D	Keratotic changes	14	2.27
3.	ECA	53	8.62
3.A	ECA-squamous	4	0.65
3.A.1	ASCUS	21	3.41
3.A.2	LSIL	2	0.32
3.A.3	ASC-H	5	0.81
3.A.4	HSIL	14	2.28
3.A.5	Squamous cell carcinoma	3	0.49
3.B	ECA-glandular	7	1.14
3.B.1	Atypical glandular cells (NOS)	6	0.97
3.B.2	Atypical endocervical cells (NOS)	1	0.16
4.	Other malignant neoplasm	1	0.16

LSIL: Low grade squamous intraepithelial lesion, HSIL: High grade squamous intraepithelial lesion, ASC-H: Atypical squamous cells, cannot exclude HSIL, ASCUS: Atypical squamous cell of undetermined significance, ECA: Epithelial Cell Abnormality

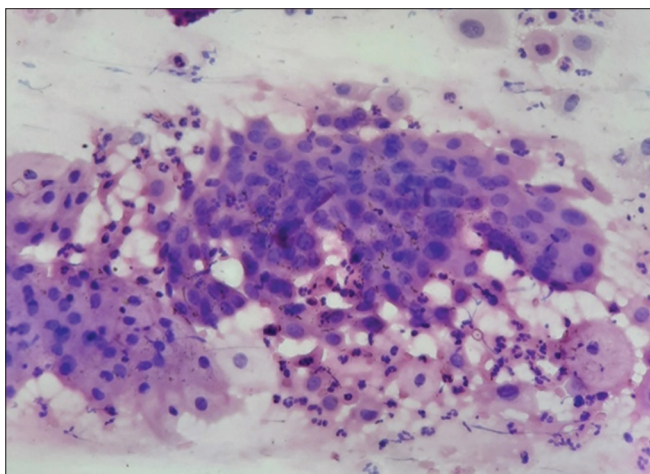


Figure 1: Atypical squamous cells of undetermined significance (×10)

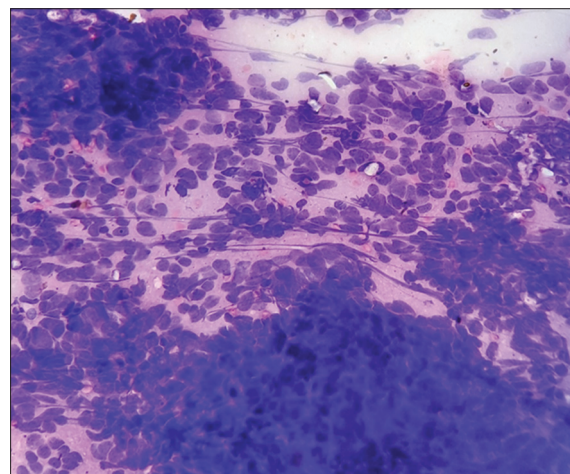


Figure 3: Squamous cell carcinoma (×10)

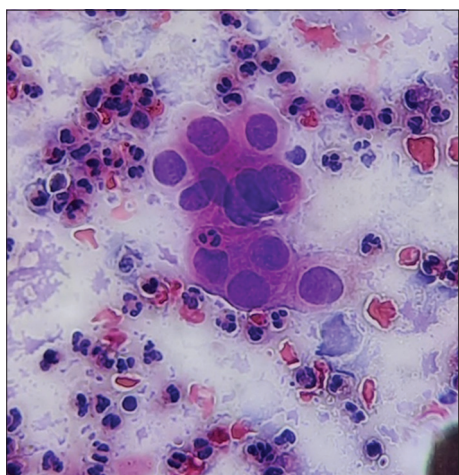


Figure 2: High-grade squamous intraepithelial lesion (×40)

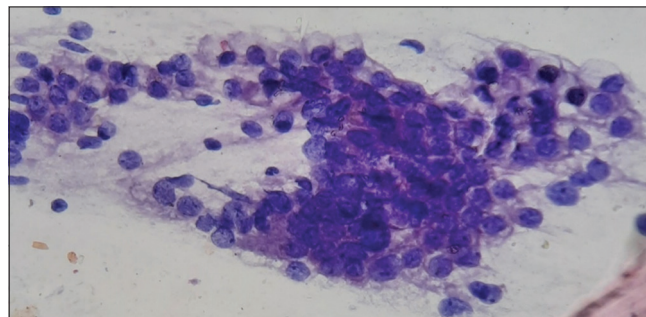


Figure 4: Atypical glandular cells (NOS) (×40)

cases, 10 cases were diagnosed as SCC and four cases were diagnosed as cervical intraepithelial neoplasia-I. Of the five ASC-H cases, on histopathology three cases were chronic cervicitis and two cases were cervical intraepithelial

neoplasia-II. Of the two LSIL cases, on histopathology, one case was chronic cervicitis and the other was cervical intraepithelial neoplasia I. The three SCC cases on Pap smear correlated on histopathology. Of the six AGCs Pap smears, four cases were reported as chronic cervicitis, and two cases as SCC. Three unsatisfactory smears which were clinically suspicious were correlated with histopathology as cervical intraepithelial neoplasia-I, benign endocervical polyp and endocervical adenocarcinoma (Table 2).

DISCUSSION

India contributes to the worldwide cervical cancer burden with 97,000 cases and 60,000 deaths.⁸ Pre-cancerous lesions can be detected by cervical cancer screening programs, and can be treated by low-cost procedures.⁹ Cervarix vaccine gives protection against oncogenic genotypes (types 16 and 18) which contribute to 70% of carcinoma cervix.¹⁰ This study evaluated the spectrum of cervical lesions on cytology and correlated the abnormal cases with histopathology on cervical biopsy.

In a study conducted by Sinchana et al., in 2022, there were seven unsatisfactory cases (3.5%) while in this study the number of unsatisfactory smears was 37 (6%).¹¹ This can be due to improper collection techniques or lack of proper transport. Associated clinical symptoms at the time of collection like bleeding per vaginum or lack of co-operation of the patients during the collection procedure may be one of the contributory factors to unsatisfactory smears. Proper collection techniques and diligent transport of slides will ensure the efficacy of the cervical screening test and better patient care.

In a study conducted by Pandey et al., in 2023, 1987 cases (93.2%) were reported as Negative for Intraepithelial Lesion or Malignancy, which was a line in this study, where 525 cases (91%) were reported as Negative for Intraepithelial Lesion or Malignancy.¹² In the study conducted by Sinchana et al., 139 cases (69.5%) were

smears associated with inflammation, whereas in this study, 353 cases (57.4%) were inflammatory smears.¹¹ Cases with persistent inflammation must be further evaluated and treated appropriately as they may slowly transform into pre-malignant lesions.¹³

In the study conducted by Pandey et al., 79 cases (3.7%) were atrophic smears, which was in line with this study, where 23 cases were (3.9%) atrophic smears.¹² In the study conducted by Sinchana et al., 18 cases (9%) were reported as ECA, which were in line with this study, where 53 cases (9%) were also reported as ECA.¹¹

In a study conducted by Sharma et al., in 2021, the total number of ASCUS cases was 15 (3.3%), which was in line with this study where 21 cases (3.74%) were reported as such.¹⁴ The same study reported five cases (1.2%) as LSIL, whereas in our study, two cases (0.32%) were reported as LSIL.¹⁴ This can be due to the challenges in diagnosing LSIL lesions due to the mild cellular changes, which can be easily missed during evaluation. Although studies have shown that only 1.5% of the women with LSIL developed cervical intraepithelial neoplasia 3, follow-up must be stringent.¹⁵ The same study reported 58 cases (13%) as ASC-H, whereas in our study only five cases (0.81%) were reported.¹⁴ Cases that are suspicious for ASC-H must be thoroughly screened and reported as they have a higher predictive value to detect cervical intraepithelial neoplasia 2 or cervical intraepithelial neoplasia 3¹⁶ (Table 3).

The same study reported two cases (0.4%) as HSIL, whereas the current study reported 14 cases (2.28%).¹⁴ This can be due to the clear-cut nuclear and cellular changes which can easily be appreciated and diagnosed on smears. The high number of cases can also be due to the late presentation of the cases due to a lack of awareness and poor implementation of screening programs. The same study also reported one case (0.2%) of SCC on pap smears, which was in line with this study where three cases (0.49%) were reported as SCC.¹⁴

Table 2: Cyto-histopathological correlation of Epithelial Cell Abnormality category cases

Bethesda category	Chronic cervicitis	Benign endocervical Polyp/hyperplasia	Cervical intraepithelial neoplasia I	Cervical intraepithelial neoplasia II/III	Squamous cell carcinoma	Adenocarcinoma	Total
ASCUS	12	4	5	-	-	-	21
ASC-H	3	-	-	2	-	-	5
LSIL	1	-	1	-	-	-	2
HSIL	-	-	4	-	10	-	14
SCC	-	-	-	-	3	-	3
AGC NOS	4	-	-	-	2	-	6
Unsatisfactory	-	1	1	-	-	1	3
Total	20	5	11	2	15	1	54

LSIL: Low-grade squamous intraepithelial lesion, HSIL: High-grade squamous intraepithelial lesion, ASC-H: Atypical squamous cells, cannot exclude HSIL, ASCUS: Atypical squamous cell of undetermined significance, SCC: Squamous cell carcinoma, AGC: Atypical glandular cells

Table 3: Review of literature-comparative analysis

Category	Sharma et al., 14(2021) (%)	Sinchana et al., 11(2022) (%)	Pandey et al., 12(2023) (%)	Present study (%)
Total number of cases	450	200	2133	615
Mean age	45	41.4	35.6	45
Most common complaint		Vaginal discharge	Vaginal discharge	Vaginal discharge
Most common speculum finding		No gross pathology		Cervical erosion
Unsatisfactory	1.7	3.5	3.47	6.02
NILM	91.3	87.5	93.2	91
Inflammation associated	79.3	69.5	33.5	57.4
Atrophic	0.9	4.5	3.7	3.9
Koilocytic/human papillomavirus induced				2.28
Squamous metaplasia				0.65
ECA	6.9	9	3.28	9
ASCUS	3.3	1	2.06	3.74
ASC-H	13	0.5	0.14	0.81
LSIL	1.2	1	0.52	0.32
HSIL	0.4	2	0.23	2.28
SCC	0.2	3.5	-	0.49
Atypical glandular cells (NOS)	0.6	1	0.33	0.97
Other malignancies	-	-	-	0.16

LSIL: Low-grade squamous intraepithelial lesion, HSIL: High-grade squamous intraepithelial lesion, ASC-H: Atypical squamous cells, cannot exclude HSIL, ASCUS: Atypical squamous cell of undetermined significance, SCC: Squamous cell carcinoma

In a study conducted by Sinchana et al., two cases (1%) were reported as AGCs (NOS), which was in line with this study where seven cases (0.97%) were also reported as AGCs (NOS).¹¹ In this study, one case was reported as poorly differentiated malignancy on pap smear, whereas no such cases were reported in the comparative studies.^{11,12,14}

Histopathological examination was advised for all ECA category cases and for those cases that were clinically suspicious though unsatisfactory on cytology. Fifty-four cervical biopsies were done. Strict follow-up of the patients, prevents attrition during the subsequent check-up. Increasing awareness of the incidence of cervical cancer in the general population also ensures follow-up.

Of the 14 cases reported as HSIL on pap smears, 10 cervical biopsies were diagnosed with SCC (71.4 % correlation), which was in line with a study by Gothwal et al., where HSIL showed an 88.89% correlation.¹⁷ All three SCC cases reported on pap smears, correlated on histopathology (100% correlation). This can be due to the fact that high-grade cervical lesions are easier to diagnose due to the high-grade nuclear features, necrosis, and clinical presentation, hence showing a higher histopathological correlation.

Three unsatisfactory Pap smears were followed up with a cervical biopsy due to clinical suspicion of abnormal lesions. On histopathology, they were diagnosed as cervical intraepithelial neoplasia 1, benign endocervical polyp, and endocervical adenocarcinoma. This reveals the importance of advising cervical biopsy even when cytology is inconclusive.

Limitations of the study

This study included only a small number of patients from one institution, hence limiting the generalizability of the findings. Studies with a larger sample size and prolonged follow-up are required to reiterate the findings.

CONCLUSION

Conventional Pap smears can help diagnose premalignant and malignant cervical lesions. Even in the absence of a high resource setup, this simple yet effective screening tool can help diagnose patients who at risk and those with frank cervical malignant lesions and reduce disease burden in the population. It can also identify inflammatory lesions which can guide the clinician to prescribe appropriate antibiotics and follow-up on the case. Strict follow-up of all abnormal cervical pap smears must be emphasized as there is a high cyto-histopathological correlation for high-grade cervical lesions. Increasing the awareness of cervical cancer in the population is crucial for reducing the incidence of the disease. This can be done by proper implementation of cervical cancer screening programs and by educating young women on the importance of regular gynecological checkups.

ACKNOWLEDGMENTS

The authors are thankful to the staff of the Department of Pathology, Government Medical College, Suryapet, Telangana.

REFERENCES

- Mustafa WA, Halim A, Jamlos MA and Idrus SZ. A review: Pap smear analysis based on image processing approach. *J Phys Conf Ser.* 2020;1529(2):022080.
<https://doi.org/10.1088/1742-6596/1529/2/022080>
- Bhatla N, Meena J, Kumari S, Banerjee D, Singh P and Natarajan J. Cervical cancer prevention efforts in India. *Indian J Gynecol Oncol.* 2021;19(3):41.
<https://doi.org/10.1007/s40944-021-00526-8>
- Ahmed NU, Rojas P and Degarege A. Knowledge of cervical cancer and adherence to Pap smear screening test among female university students in a multiethnic institution, USA. *J Natl Med Assoc.* 2020;112(3):300-307.
<https://doi.org/10.1016/j.jnma.2020.03.007>
- Thomson KA, Sandoval M, Bain C, Holme F, Bansil P, Figueroa J, et al. Recall efforts successfully increase follow-up for cervical cancer screening among women with human papillomavirus in Honduras. *Glob Health Sci Pract.* 2020;8(2):290-299.
<https://doi.org/10.9745/GHSP-D-19-00404>
- Pangarkar MA. The Bethesda system for reporting cervical cytology. *Cytojournal.* 2022;19:28.
https://doi.org/10.25259/CMAS_03_07_2021
- Goyal A, Patel AP, Dilcher TL and Alperstein SA. Effects of implementing the dual Papanicolaou test interpretation of ASC-H and LSIL following Bethesda 2014: A retrospective comparison with LSIL-H and ASC-H. *Am J Clin Pathol.* 2020;154(4):553-558.
<https://doi.org/10.1093/ajcp/aqaa069>
- Dasgupta S. The efficiency of cervical Pap and comparison of conventional Pap smear and liquid-based cytology: A review. *Cureus.* 2023;15(11):e48343.
<https://doi.org/10.7759/cureus.48343>
- Arbyn M, Weiderpass E, Bruni L, de Sanjosé S, Saraiya M, Ferlay J, et al. Estimates of incidence and mortality of cervical cancer in 2018: A worldwide analysis. *Lancet Glob Health.* 2020;8(2):e191-e203.
[https://doi.org/10.1016/S2214-109X\(19\)30482-6](https://doi.org/10.1016/S2214-109X(19)30482-6)
- Dykens JA, Smith JS, Demment M, Marshall E, Schuh T, Peters K, et al. Evaluating the implementation of cervical cancer screening programs in low-resource settings globally: A systematized review. *Cancer Causes Control.* 2020;31(5):417-429.
<https://doi.org/10.1007/s10552-020-01290-4>
- Cheng L, Wang Y and Du J. Human papillomavirus vaccines: An updated review. *Vaccines (Basel).* 2020;8(3):391.
<https://doi.org/10.3390/vaccines8030391>
- Sinchana KM, Jadhav MN and Kittur SK. Cytomorphological study of cervical Pap smear based on the Bethesda system 2014. *Indian J Pathol Oncol.* 2022;9(3):232-237.
<https://doi.org/10.18231/j.ijpo.2022.055>
- Pandey D, Mondal SK, Santosh T, Saha R, Mazumder S and Chakrabarti I. A retrospective study on cervical cancer screening in a newly opened tertiary care Centre in Eastern India. *IP J Diagn Pathol Oncol.* 2023;8(2):83-88.
<https://doi.org/10.18231/j.jdpo.2023.018>
- Shrestha J, Magar DG and Pandey C. Cervical intraepithelial lesions in women with persistent inflammatory smear on Pap smear: A descriptive cross-sectional study. *JNMA J Nepal Med Assoc.* 2021;59(241):848-852.
<https://doi.org/10.31729/jnma.7011>
- Sharma HB, Bansal M, Kumar N and Gupta M. Spectrum of Pap smear cytology in women presenting in a tertiary care center in North India-a two year study. *IP Arch Cytol Histopathol Res.* 2021;6(1):7-11.
<https://doi.org/10.18231/j.achr.2021.002>
- Bruno MT, Cassaro N, Bica F and Boemi S. Progression of CIN1/LSIL HPV persistent of the cervix: Actual progression or CIN3 coexistence. *Infect Dis Obstet Gynecol.* 2021;2021:6627531.
<https://doi.org/10.1155/2021/6627531>
- Kattoor J and Kamal MM. The gray zone squamous lesions: ASC-US/ASC-H. *Cytojournal.* 2022;19:30.
https://doi.org/10.25259/CMAS_03_10_2021
- Gothwal M, Singh P, Elhence P, Yadav G, Sharma C and Samriya N. Spectrum of abnormal cervical lesions and its cytohistological correlation: A study from an institute of national importance of Western Rajasthan. *Maedica.* 2022;17(3):636-640.
<https://doi.org/10.26574/maedica.2022.17.3.636>

Authors Contribution:

MMT- Concept and design of the study, results interpretation, review of literature, and preparing first draft of manuscript. Statistical analysis and interpretation, revision of manuscript; **SB**- Concept and design of the study, results interpretation, review of literature and preparing first draft of manuscript, revision of manuscript; **MEM**- Review of literature and preparing first draft of manuscript. Statistical analysis and interpretation; **SRA**- Concept and design of the study, results interpretation, review of literature and preparing first draft of manuscript. Statistical analysis and interpretation, revision of manuscript; **AJ**- Concept and design of the study, results interpretation, review of literature and preparing first draft of manuscript. Statistical analysis and interpretation, revision of manuscript; **HK**- Review of literature; **DSR**- Review of literature.

Work attributed to:

Government Medical College, Suryapet, Telangana.

Orcid ID:

Meghna Maria Tharakan - <https://orcid.org/0000-0002-1722-1761>
 Sandhya Bangaru - <https://orcid.org/0009-0001-4857-9440>
 M. Mark Edward - <https://orcid.org/0009-0002-2923-3214>
 A. Smita Reddy - <https://orcid.org/0009-0005-5571-3360>
 Anunayi Jeshtadi - <https://orcid.org/0009-0007-0895-4879>
 Harika Kalangi - <https://orcid.org/0000-0001-9298-9028>
 Danda Samyukta Reddy - <https://orcid.org/0009-0003-2069-3588>

Source of Support: Nil, **Conflicts of Interest:** None declared.