



DETECTION OF ABNORMAL CERVICAL CYTOLOGY BY LBC (LIQUID BASED CYTOLOGY)

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ABSTRACT **Introduction:** Cancer cervix is the fourth most common cancer among women globally. It is responsible for 7.7% of all female cancer death. It takes around 15-20 years in normal immunity patients and 5-10 years in immune-compromised patients to convert precancerous lesions of the cervix into cancer cervix. Cervical cytology plays a very important role in the early diagnosis and management of these precancerous lesions to improve prognosis. quite low Pap smear sensitivity, in the range of 50%, but as low as 20% has been reported by some recent meta-analysis studies. LBC was introduced in the mid-1990s as an alternative technique to process cervical smear samples for cytological evaluation. Studies of the accuracy of liquid-based preparations reports sensitivity of 61-66% and specificity of 82-91%. **Materials And Methods:** A retrospective study was done at a private clinic and pathology lab in District Shivpuri (MP) from 1st October 2020 to 30th November 2022 on 760 patients. Inclusion criteria:-Patients in the age group of 21-65 years with complaints of abnormal vaginal discharge, intermenstrual bleeding, postmenopausal bleeding, post-coital bleeding, dyspareunia, foul-smelling discharge, backache, and Lower abdominal pain were included in this study. Sample was taken with Broom, and Cyto-brush from the transformation zone and endocervix and placed in liquid fixative buffered methanol solution and send to the pathology lab. **Results** Most of the patient 42% were between 31-40 years of age group. The majority 48.42% of them were educated up to High school. Most of them 84.07% were from rural back ground, multiparous 86.05%, and married 99.73%. 25% of women visited OPD with complaints of abnormal vaginal discharge followed by menstrual abnormalities in 20.79%, other complaints were, Pain abdomen 16.97%, Vulval itching 12.11%, Low back pain 3.95%, Dyspareunia 3.03% and others 5.13%. (Loss of weight and appetite, STD/genital warts) 9.08% women came for routine checkup. The most common finding on per speculum examination was Cervical ectopy in 33.95%. Normal cervix was found in 26.05%. Other findings on Per-speculum examination were, Hypertrophied cervix, Inflammation, Cervical Polyp, UV Prolapse/ cystocele, Cervical Ulcer, Cervix flushed with the vagina and Cervical growth in 20%, 9.08%, 4.34%, 4.61%, 3.03%, 0.13% and 0.13% respectively. Out of 760 cases, 61.05% of patients were reported as negative for intraepithelial lesion (NILM). The most common non-neoplastic cytological finding was an inflammatory smear in 25.00% of cases. Various Infections were found in 6.18% of cases, and epithelial cell abnormalities were found in 3.42% of cases. The most common abnormalities were ASC-US 0.92% and ASC-H 0.92%, followed by LSIL 0.53%, HSIL 0.66%, AGUS 0.26%, and SCC 0.13%. Bacterial vaginosis 2.37% was the most common infective organism found in cytology followed by Candida albicans 1.97%, Trichomonas vaginalis 1.71%, and Herpes simplex virus 0.13%. **Conclusion** The cytology-based screening program is still the mainstay in the early diagnosis of cancer cervix. To improve diagnostic accuracy as sensitivity and specificity in the field of cervical cytology, Liquid-based cytology (LBC) is preferred. Its advantages over conventional Pap smears include proper visualization of cellular features due to a reduction in air-drying artifacts and reduced number of unsatisfactory smears. The residual specimens from the LBC technique can be used to detect human papillomavirus DNA through immune-cytochemistry if needed. thus, LBC is recommended as a cervical cytology screening tool to achieve the WHO elimination strategy.

KEYWORDS : Liquid-based cytology, Cytology-based screening, precancerous lesions

INTRODUCTION

Cancer cervix is the fourth most common cancer among women globally. It is responsible for 7.7% of all female cancer death. Its global incidence is 13.3 cases/ 1 lac women with a mortality rate of 7.7 deaths/1 lac women.¹ Indian incidence of cancer cervix is 18 cases/1 lac women, being 2nd most common female cancer In India and the most common female cancer in Indian rural areas. It is responsible for 11.4% of all cancer deaths reported annually in India.

It takes around 15-20 years in normal immunity patients and 5-10 years in immune-compromised patients to convert precancerous lesions of the cervix into cancer cervix. Cervical cytology plays a very important role in the early diagnosis and management of these precancerous lesions to improve prognosis. With regular cytology screening programs, a major decline in cervical cancer incidence and mortality is reported in developed countries^{2,3,4} but it remains largely uncontrolled in high-risk developing countries because of ineffective or no screening program.^{5,6,7,8}

The Papanicolaou (Pap) smear is the most commonly used screening test for cervix cancer for the last 50 years,⁹ but accuracy of this important screening test remains controversial. Quite low Pap smear sensitivity, in the range of 50%, but as low as 20%¹⁰ has been reported by some recent meta-analysis studies. Poor sensitivity of pap smear may be due to errors in sampling, preparation, and interpretation. Sampling errors can occur due to too small lesion, failure of the device (spatula) to pick up cells, or inadequate transfer of cells to glass slide as they remain in pores of a wooden spatula, while preparation errors may occur due to poor fixation (air drying artifact), presence of blood and

mucous in background and errors in spreading leading to the variable thickness of the cellular component. Interpretation errors can also occur due to failure to detect abnormal cells on a slide. Hence to improve sensitivity and to decrease false negative results, other methods have been introduced as given below.

LBC was introduced in the mid-1990s as an alternative technique to process cervical smear samples for cytological evaluation. Reviews of published studies indicate that liquid-based cytology is probably more sensitive than Pap smear in detecting cervical neoplasia and it improves sample adequacy.¹¹ Studies of the accuracy of liquid-based preparations reports sensitivity of 61-66% and specificity of 82-91%. ThinPrep (LBC) was significantly more sensitive than the conventional smears for detecting high-grade squamous intraepithelial lesions (HSIL) and cancer, with sensitivity rates of 92.9% and 100% vs 77.8% and 90.9%, respectively (P<0.001).¹²

The sample of LBC is collected in the same manner as it used to be in the conventional Pap test. A plastic spatula (in place of wooden in Pap smear) can be used. Broom and cyto-brush are the most effective sampling device to collect ectocervical and endocervical cells. However, rather than smearing the cytological sample directly onto a microscopic slide, cells are suspended in a liquid fixative (buffered methanol solution). This removes blood, mucus, and inflammatory cells. The suspended cells are then gently sucked onto a filter membrane and filter is pressed upon a glass slide to form a thin monolayer smear, and then it is stained. Two FDA-approved tests are available for LBC 1. Sure Path: The sample is taken like for a normal pap smear with a special plastic spatula and endo-cervical brush

(Cervix brush- combi), then tip is broken off by rotating the device and sent to laboratory in liquid medium only. 2. Thin prep: In this method sample is taken with a plastic broom like a normal pap smear (see above) or with a cervix brush combi, the device (broom) is immediately and vigorously agitated (shaken) in the liquid medium. The device is then discarded and the material sent to laboratory. LBC is proposed to have many benefits over conventional Pap smear such as less number of unsatisfactory (U/S) smears.¹³ Immediate fixation with enhanced nuclear and cytoplasmic details as fewer artifacts in cellular morphology e.g. Nuclear feathering artifact, More representative transfer of cells from the collecting device (cells are lost during the collection with a wooden Ayer spatula in Pap smear), evenly distributed cellular material in a thin layer over a fixed area so screening time reduced, Clear background so less obscuring inflammatory cells, mucous, blood and debris, so fewer chances for epithelial cells of interest to be obscured, using residual cellular material for human papillomavirus (HPV) testing, and a possibly higher rate of high grade squamous intraepithelial lesion (HSIL) detection, multiple samples can be prepared as necessary, LBC slides are suitable for automated analysis.

Some Disadvantages of LBC are-Dispersion of abnormal cells, altered smear pattern due to randomization of cells, loss of relationship between cells which may cause loss of diagnostic clue, some epithelial cells round up and appear smaller with the appearance of altered/increased nuclear -cytoplasmic ratio. This first-generation LBC technology is expensive as it requires an automated instrument.

A new second-generation technique, Liqui prep was introduced after a decade after the advent of liquid-based cytology, this had the advantage of a much lower cost. However, the information available on the second generation LBC is limited.

MATERIALS AND METHODS

A retrospective study was done at a private clinic and pathology lab in District Shivpuri (MP) from 1st October 2020 to 30th November 2022 on 760 patients

Inclusion Criteria:-

Patients in the age group of 21-65 years with complaints of abnormal vaginal discharge, intermenstrual bleeding, postmenopausal bleeding, post-coital bleeding, dyspareunia, foul-smelling discharge, backache, and Lower abdominal pain were included in this study.

Exclusion Criteria:-

Women with invasive cervical cancer and those who are not giving consent for liquid base cytology were excluded from the study.

In this study, the results of liquid base cytology collected from 760 women were studied. Data was collected from the reports and records from the clinic and pathology lab and analyzed for detailed history, personal information such as age, literacy, socioeconomic status, parity, marital status, various complaints, associated high-risk factor, clinical findings, and other relevant information. Reporting was done according to the guidelines of the 2014 Bethesda system.

Technique- Before taking cervical smear, vaginal examination was performed. Women were advised to abstain from intercourse, douching and any medicinal cream application for at least 24 hours before the test, the patient was placed in the dorsal position and a Cusco speculum was inserted, Sample was taken with Broom, and Cyto-brush from the transformation zone and endocervix and placed in liquid fixative buffered methanol solution and send to the pathology lab.

A total of 760 cases were included in this study and their data were analyzed using IBM SPSS ver.20 software. Frequency distribution and cross-tabulation were used to prepare tables and data expressed as percentages.

RESULTS

Table 1- Socio-demographic Characteristics. (n=760)

Age Group (years)	No. of cases	(%)
<21-30	69	9.08
31-40	319	41.97
41-50	228	30.00
51-60	114	15.00
>61	30	3.95
Total	760	100

Educational level		
Illiterate	35	4.61
Primary	112	14.74
Middle	96	12.63
High school	368	48.42
Graduation	104	13.68
Post Graduation	45	5.92
Total	760	100
Residence		
Rural	639	84.08
Urban	121	15.92
Total	760	100
Parity		
Nulliparous	23	3.03
Primiparous	83	10.92
Multiparous	654	86.05
Total	760	100
Material Status		
Married	758	99.74
Unmarried	2	0.26
Total	760	100

Most of the patient 42% were between 31-40 years of age group. The majority 48.42% of them were educated upto High school. Most of them were from rural background 84.08%, multiparous 86.05%, and married 99.74%.

Table 2- Presenting Complaints (n=760)

COMPLAINTS	Number	Percentage	
Routine checkup	69	9.08	
Abnormal vaginal discharge	190	25.00	
Pain abdomen	129	16.97	
Post-coital bleeding	30	3.95	
Menstrual abnormalities 20.79%	Post-menopausal bleeding	45	20.79
	Prolong and Heavy Menstrual period	53	
	Inter menstrual bleeding	60	
Low back pain	30	3.95	
Vulval itching	92	12.11	
Dyspareunia	23	3.03	
Others (Loss of weight and appetite, STD/genital warts)	39	5.13	
Total	760	100	

Most of the women 25% visited OPD with complaints of abnormal vaginal discharge followed by menstrual abnormalities in 20.79%, other complaints were, Pain abdomen at 16.97%, Vulval itching 12.11%, Low back pain 3.95%, Dyspareunia 3.03% and others 5.13%. (Loss of weight and appetite, STD/genital warts) 9.08% women came for a routine checkup.

Table 3- Vaginal Per Speculum Examination Findings

Finding	NO	Percentage
Normal cervix	198	26.05
Hypertrophied cervix	152	20
Cervical ectopy	258	33.95
Ulcer	23	3.03
Polyp	33	4.34
Inflammation	59	9.08
UV Prolapse/ cystocele	35	4.61
Cervix flushed with vagina	1	0.13
Cervical growth	1	0.13
Total	760	100

The most common finding 33.95% on per speculum examination was Cervical ectopy. Normal cervix was found in 26.05%. Other findings on Per-speculum examination were, Hypertrophied cervix, Inflammation, Cervical Polyp, UV Prolapse/ cystocele, Cervical Ulcer, Cervix flushed with the vagina and Cervical growth in. 20%, 9.08%, 4.34%, 4.61%, 3.03%, 0.13% and 0.13% respectively.

Table 4- LBC Findings

Cytology report	Number	Percentage
NILM	464	61.05
Inflammatory	190	25.00
Atrophic	33	4.34
Infections	47	6.18
Epithelial cell abnormalities	26	3.42
Total	760	100

Out of 760 cases, 61.05% of patients were reported as negative for intraepithelial lesion (NILM). The most common non-neoplastic cytological finding was inflammatory smear in 25.00% of cases. Various Infections were found in 6.18% of cases, and epithelial cell abnormalities were found in 3.42% of cases.

Table 5 Epithelial Cell Abnormality (n=26)

Epithelial cell abnormality	Number	(%)
ASC-US	7	0.92
ASC-H	7	0.92
LSIL	4	0.53
HSIL	5	0.66
AGUS	2	0.26
SCC	1	0.13

ASC-US: Atypical squamous cells of undetermined significance; ASC-H: Atypical squamous cells; that cannot rule out high-grade lesion; AGUS Atypical glandular cell of undetermined significance LSIL: Low-grade squamous intraepithelial lesion; HSIL- High grade squamous intraepithelial lesion; SCC: Squamous cell carcinoma.

The most common abnormalities were ASC-US 0.92% and ASC-H 0.92%, followed by LSIL 0.53%, HSIL 0.66%, AGUS 0.26%, and SCC 0.13%.

Table 6 Types Of Infections (n=47)

Infectious organism	Number	(%)
Bacterial vaginosis	18	2.37
Candida albicans	15	1.97
Trichomonas vaginalis	13	1.71
Herpes simplex virus	1	0.13

Bacterial vaginosis was the most common infective organism found in 2.37% on cytology followed by Candida albicans 1.97%, Trichomonas vaginalis 1.71%, and Herpes simplex virus 0.13%.

DISCUSSION:

Liquid-based cytology (LBC) is a cervical cancer screening technique that inspects cells by dissolving them in liquid. This method is less invasive than the conventional Pap smear test. The most important benefit of LBC consist of, a probable increase in prediction of high-grade cervical intra epithelial neoplasia (CIN), reduction in the number of unsatisfactory smears, most of the collected cellular material is available for laboratory processing, and the residual specimens can be used for HPV DNA testing.¹⁴

This was a retrospective study done in a private clinic and pathology lab in District Shivpuri (MP) the study was done during the period from 1st October 2020 30th November 2022.

A total of 760 cases were analyzed during study period. Different cases were studied and all the data were analyzed using IBM SPSS ver.20 software.

In our study, most (42%) of the patient were between 31-40 years of age group. Sangeetha A et al¹⁵ analyzed 310 cases of cervical lesions. The most common age group was between 31-40 years (39%). In a study conducted by Singh A et al¹⁶, a maximum number of cases were noted between 31 and 40 years. Similar finding of a maximum number of patients presenting to the age group of 30-35 years were observed by Siebers et al¹⁴ and Ranjana H et al¹⁷.

In this study, 47.1% of cases belonged to the lower socioeconomic groups and majority 48.42% of them were educated upto HSC. In a study done by Khaengkhor P et al¹⁸, 66% of patients had completed the secondary level education and 89% belonged to lower socioeconomic group.

In our study, most of them were of rural back ground (84.07%), multiparous (86.05%) and married (99.73%). According to a study

done by Tesfaw et al¹⁹ (74.88) of women were married and maximum women were multigravida (75%). According to Pragya Shree et al²⁰, total of 66% subject belonged to lower socioeconomic status. Another study done by Savithri DR et al²¹ showed that 94% women were married. Vallikad E et al²² and Kurkure AP et al²³ concluded that in India women of low socio economic class and rural women showed higher incidence of cancer cervix. The main explanation specified for this is lack of access to screening and health services and poor knowledge about the risk factors of cancer cervix. These findings are almost similar to our study.

In this study, most 25.00% of the women visited OPD with complaints of abnormal vaginal discharge followed by menstrual abnormalities 20.79%, other complaints for that women were visited in clinic were routine checkup in 9.08%, Pain abdomen in 16.97%, Low back pain in 3.95%, Vulval itching 12.11%, Dyspareunia in 3.03% and Others (Loss of weight and appetite, STD/genital warts) in 5.13%. Sherwani et al²⁴ analyzed 160 patients with cervical lesions, the most common complaint was white discharge in 42.5% of cases, followed by pain abdomen (27.5%) and menstrual irregularity in 23.8% of cases. Similar finding were observed by Afshan N et al²⁵, they also found that most common presenting complaints in their study was white discharge per vagina, in (42.5%) cases.

The most common finding on perspeculum examination in our study was Cervical ectopy in 33.95%, normal cervix was found in 26.05%, unhealthy with erosion in 13.95%, congested and hypertrophied cervix in 20.00%, UV Prolapse/ cystocele in 3.95% of cases. Cervix was flushed with vagina in 1.05% and Cervical growth was in 1.05% of cases. In a study conducted by Singh S et al²⁶, most common per speculum finding was cervical erosion in 60%. Patel S et al²⁷ found that P/S findings were normal in 52 and abnormal in 20 cases. It was erosion Cx in 4, hypertrophied Cx in 4, hypertrophied Cx in 3, ulcer Cx in 1 and papillary growth in 1.

Out of 760 cases in this study, 61.05% of patients were reported as negative for intraepithelial lesion (NILM). The most common non neoplastic cytological finding was inflammatory smear in 25.00% of cases. Various Infections were found in 6.18% of cases, Epithelial cell abnormalities were found in 3.42% of cases. In the study by Sangeetha A et al¹⁵, NILM-normal detected on LBC was (64.84%). Inflammatory smears on LBC were 22.9%. NILM-Atrophic smears were (6.77%). Another study done by Sharma J et al²⁸ showed that 40% patients had NILM and inflammatory smears were seen in 20% of cases. Singh S et al²⁶ in their study concluded that 28.7% had inflammatory smears and % of NILM in LBC was (46.25%). Ranjana H et al¹⁷ also observed that % of NILM was (80.6%) These findings are in accordance with our study.

In this study, most common abnormalities were ASC-US 0.92% and ASC-H 0.92%, followed by LSIL 0.53%, HSIL 0.66%, AGUS 0.26% and SCC 0.13%. In a study conducted by Sangeetha A et al¹⁵, ASCUS was 2.26% on LBC. ASC-H detected was 0.32%. LSIL was 0.65% on LBC. This was in cordance with study of Colgan TJ et al²⁹ which also showed an increasing trend in detection of ASCUS by 0.88%, LSIL by 0.63% and HSIL by 0.03% on LBC. Park J et al³⁰ also observed increasing trend in detection of ASCUS by 3.9%, LSIL by 4.3% and HSIL by 1.9%.

Infectious organisms found during the study were Trichomonas vaginalis, Candida albicans, Bacterial vaginosis and Herpes simplex virus. Bacterial vaginosis 2.37% was the most common infective organism found in cytology followed by Candida albicans 1.97%, Trichomonas vaginalis 1.71%, and Herpes simplex virus 0.13%. In a study conducted by Singh S et al²⁶, the most common infectious organisms were bacterial vaginosis (10.81%), Trichomonas vaginalis (16.21%) and candida albicans (13.51%). Another study done by Anushree CN et al³¹ concluded that Candida albicans (3.2%), bacterial vaginosis (2.8%) and trichomonas vaginalis (0.8%) were the three most common infectious organisms found in their study. A study conducted by Savithri DR et al²¹ revealed that infectious organisms noted during the study were Trichomonas vaginalis, Candida albicans, Bacterial vaginosis and Herpes simplex virus. The incidence of candida albicans (10%) being the highest amongst the various infectious organisms noted followed by Trichomonas vaginalis (2%). Bacterial vaginosis and Herpes simplex virus accounted for 1% each

CONCLUSION

WHO strategy is 90:70:90 for elimination of cervix cancer by

2030(elimination criteria is cervical cancer incidence ≤ 4 per 100,000 women worldwide) through the triple-intervention strategy of 1) vaccinating 90% of all girls by age 15 years, 2) screening 70% of women twice in the age range of 35 to 45 years, and 3) treating at least 90% of all precancerous lesions detected during screening. This can be easily achieved by combined vaccination and screening strategy, which is highly cost effectiveness across countries, as it takes several years for a pre-invasive lesion to become invasive and incurable. Early diagnosis of cancer in the pre-invasive state has a better prognosis and advanced-stage morbidity and mortality can be prevented. The cytology-based screening program is still the mainstay in the early diagnosis of cancer cervix. To improve diagnostic accuracy as sensitivity and specificity in the field of cervical cytology, Liquid-based cytology (LBC) is preferred. Its advantages over conventional Pap smears include proper visualization of cellular features due to a reduction in air-drying artifacts and obscuring background elements thus reducing the number of unsatisfactory smears. The residual specimens from the LBC technique can be used to detect human papillomavirus DNA through immunocytochemistry if needed. Thus, LBC is recommended as a cervical cytology screening tool to achieve the WHO elimination of cancer cervix.

REFERENCES

1. GLOBAL CANCER OBSERVATORY, GLOBOCAN 2020 REPORT
2. International Agency for Research on Cancer (IARC). Handbooks of Cancer Prevention. Volume 10 Cervix Cancer Screening. IARC Press; 2005 Accessed November 23, 2020. Publications.iarc.fr/Book-And-Report-Series/Iarc-Handbooks-Of-Cancer-Prevention/Cervix-Cancer-Screening-2005
3. Bray F, Carstensen B, Moller H, et al. Incidence trends of adenocarcinoma of the cervix in 13 European countries. *Cancer Epidemiol Biomarkers Prev.* 2005;14: 2191-2199.
4. Bray F, Loos, AH, McCarron P, et al. Trends in cervical squamous cell carcinoma incidence in 13 European countries: changing risk and the effects of screening. *Cancer Epidemiol Biomarkers Prev.* 2005; 14: 677-686
5. Mallach MK, Taylor DG, Badwe RA, Rath GK, Shanta V, PrameshCS, et al. The growing burden of cancer in India: epidemiology and social context *Lancet Oncol.* 2014;15(6):205-12
6. 175 Pilleron S, Cabaasag CJ, Ferlay J, et al. Cervical cancer burden in Latin America and the Caribbean: where are we? *Int J Cancer.* 2020; 147: 1638-1648.
7. 176 Bray F, Lortet-Tieulent J, Znaor A, Brotons M, Poljak M, Arbyn M. Patterns and trends in human papillomavirus-related diseases in central and eastern Europe and central Asia. *Vaccine.* 2013;31(suppl7):H32-H45
8. 177 Jedy-Agba E, Joko WY, Liu B, et al. Trends in cervical cancer incidence in sub-Saharan Africa. *Br J Cancer.* 2020; 123: 148-154.
9. Cuzick J, Arbyn M, Sankaranarayanan R, Tsu V, Ronco G, Mayrand MH, et al. Overview of human papillomavirus-based and other novel options for cervical cancer screening in developed and developing countries. *Vaccine* 2008;26(10):29-41
10. Papanicolaou GN, Traut HF. The diagnostic value of vaginal smears in carcinoma of the uterus. *Arch Pathol Lab Med.* 1997;121 (3): 211-24
11. Strander B, Andersson-Ellstrom A, Milsom I, Radberg T Ryd, W. Liquid-based cytology versus conventional Papanicolaou smear in an organized screening program: a prospective randomized study. *Cancer* 2007;111(5):258-91.
12. Liptak, Peter; Barnetson, Robert James (2012-02-14). "Liquid-based cervical cytology in the United Kingdom and South Africa". *Continuing Medical Education.* 30 (2):L 45-48. ISSN 2078-5143
13. Nanda K, McCrory DC, Myers ER, Bastian LA, Hasselblad V, Hickey JD, et al. Accuracy of the Papanicolaou's test in screening and follow-up of cervical cytologic abnormalities; a systematic review. *Ann Intern Med.* 2000;132(10):810-3.
14. Siebers AG, Klinkhamer PJ, Arbyn M, Raifu AO, Massuger LF, Bulten J. Cytological detection of cervical abnormalities using liquid-based compared with conventional cytology. *Obstet Gynecol.* 2008;112:1327-34.
15. Sangeetha A, Subbulakshmi G, Arasi R. A comparative analysis of manual liquid based cytology versus conventional smear. *Int J Sci Res.* 2018;7(4):42-4.
16. Singh A, Joshi C, Kujur P, Chandrakar K, Shrivastava S. Liquid-based Cytology versus Conventional Cytology for Evaluation of Cervical Cytology in a Tertiary Care Center of Chhattisgarh. *Int J Sci Study.* 2016;4(9):161-7.
17. Ranjana H, Sadhna S. Comparison of conventional pap smear versus liquid based cytology in a diagnostic centre of central. Madhya Pradesh. *Indian J Pathol Oncol.* 2016;3:42-7.
18. Khaengkhon P, Mairang K, Suwannarurk K, Thaweekul Y, Poomtavum Y, Pattaraarchachai J et al. *J Med Assoc Thai.* 2011;94 (2): 152-8.
19. Tesfaw G, Ahmed Y, Gedefaw L, Dube L, Godu S, Eshetu K et al. Liquid Based Cytology for the Detection of Cervical Intraepithelial Lesions among Women in Jimma Town, Ethiopia. *BMC Cancer.* 2020;10:1-13.
20. Pragya Shree, Mittal N, Verma V. Comparison of Visual Inspection using Acetic Acid and Liquid Based Cytology for Cervical Cancer Screening in Rural Area: A Cross-sectional Study. *Journal of Clinical and Diagnostic Research.* 2021;15(3): QC14-QC18.
21. Savithri DR, Sankalpa AJ. Prevalence of abnormal cervical cytology on liquid-based cytology in women attending gynecology OPD at tertiary care center Bangalore, Karnataka. *India Int J Reprod Contracept Obstet Gynecol.* 2022;11(8):2117-21.
22. Vallikad E, "Cervical Cancer: The Indian Prospective," *International Journal of Gynecology Obstetrics.* 95(1) November 2006: S215-S233.
23. Kurkure AP, and Yeole BB, "Social inequalities in cancer with special reference to South Asian Countries," *Asian Pacific Journal of Cancer Prevention.* 7 (1) (Jan - March 2006): 36-40.
24. Sherwani RK, Khan T, Akhtar K, Zeba A, Siddiqui FA, Rahman K, et al. A comparative study of conventional pap smears and liquid based cytology. *J Cytol.* 2007;24(4):167-72.
25. Afshan N. Role of cytology, colposcopy and colposcopic directed biopsies in the evaluation of unhealthy cervix. MD Thesis. Rajiv Gandhi Univ. of Health Sciences. Bijapur. 2010.
26. Singh S, Gupta A, Nath D, Shobha HJ. A study of comparison of liquid-based cytology versus conventional pap smear for evaluation of cervical cytology at a tertiary healthcare hospital *Int J Res Med Sci.* 2019;7(5):1869-76.
27. Patel S, Modi D, Modi J. Liquid-based cytology and conventional cytology for assessment of cervical pap smear. *European J Molecular & Clin Med.* 2022;9(3):3003-7.
28. Sharma J, Toi PCh, Siddaraju N, Sundareshan M, Habeebullah S. A comparative analysis of conventional and SurePath liquid-based cervicovaginal cytology: A study of 140 cases. *J Cytol.* 2016;33(2):80
29. Colgan T. Results of the Implementation of Liquid-Based Cytology Sure Path in the Ontario Screening Program *Cancer (Cancer Cytopathol)* 2004;102:362-7.
30. Park J. Liquid-Prep Versus Conventional Pap Smear. *Diagnostic Cytopathology.* 2007;35(8):488-92.
31. Anushree CN, Priyanka S, Hugar NN, Manjunatha YA. Comparison of Conventional Pap Smears versus Liquid Based Cytology for Clinicopathological Patterns of Cervical Lesions at a Tertiary Care Centre, Bangalore, India. *National J Lab Med.* 2022;11(3): PO81-PO85.