Correlation of Cervical Pap Smear with Histo-pathological Diagnosis in Cervical Lesions: A Meta-Analysis

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Abstract: *Carcinoma cervix is one of the leading causes of death of the female population in developing countries. PAP test or PAP Smear is a screening test widely used to identify potentially pre-cancerous & cancerous lesion of the cervix. It was invented by Georgios Papanikolaou in 1920 and introduced in cervical cytological screening in 1940. Cervical lesions if treated in earlier stages, the patient can be cured of the disease because cervical cancer has very long pre-invasive stage. PAP test represents the most effective technique to prevent and detect the precancerous conditions of the uterine cervix before they becomes invasive cancer, its false negative*
yield due to the potential sampling and interpretation errors yield is still a reason of concern. In this paper we evaluate the pattern of cervical pap smear cytology and to correlate with histopathological diagnosis, to determine accuracy of pap smear, to reduce false negative results. Using internet search engines, a thorough review of the literature was conducted. Cytopathological and Histopathological correlation of cervical smears is the best way of internal quality assurance and also sometimes helpful to find out the factors responsible for discrepant cases.
Keywords: *Pap smear, Cytology, Histopathology & Cervix biopsy.*
Study Design: *Review Article.*

I. Introduction

Cancer of cervix ranks as the third common malignancy in females worldwide.[1] In developing countries like India, carcinoma cervix is the second commonest malignancy affecting females. India accounts for 18% of the global burden of carcinoma cervix. In India, every year 1,26,000 new cases are identified and 67,477 deaths occur due to cervical carcinoma[2]. Cervical carcinoma affects women of age 15-44 years and disease peaks at 55-66 years. On average, Indian women have a 2.5% risk of developing carcinoma cervix. It was estimated worldwide that every 5th woman, who suffer from cervical cancer belongs to India[3].

Carcinoma cervix is one of the leading causes of death of the female population in developing countries. According to Global cancer statistics 2018, cervical cancer is the fourth most frequent cancer in women with an estimated 570,000 new cases representing 6.6% of all female cancers.

Approximately 90% of deaths from cervical cancer occurred in low- and middle-income countries.Cervical cancer ranks fourth for both incidence (6.6%) and mortality (7.5%) [4].

By virtue of its accessibility, malignancy of the cervix can be readily diagnosed even in its pre-invasive stage. If treated in the earlier stages, the patient can often be cured of the disease. The introduction of cytological screening by *George Papanicolaou* in the late 1940s was a great public health success story in cervical cancer prevention[5].

Although Pap cytology represents the most effective technique to prevent and detect the precancerous conditions of the uterine cervix before they become invasive cancer, its false negative yield due to the potential sampling and interpretation errors yield is still a reason of concern. Thus, the final diagnosis should be made on histological examination to assess the accuracy of the cervical cytology. Cytohistopathological correlation of Pap smear is one of the recommendations of the European guidelines for quality assurance for the development of cytology laboratory performance and in particular to reduce false-negative results [6].

II. Material & Method

We conducted a thorough literature search in the PubMed and Google Scholar databases using the following keywords:- Cervix, Cytology, Cyto-pathology, Cytology-histology correlation. Included were reports in which a recognizable classification system was used to categories cervical cytology smears. Case reports and case series were not considered. Cross references in the chosen articles were also checked for additional studies. Publications having both cervical cyto-pathological & histo-pathological parameters were considered for meta-analysis. Papers that only provided statistical measures of cytology's performance (sensitivity, specificity, negative and positive predictive values) in comparison to histopathology but did not provide details on histopathological diagnoses were also excluded from the meta-analysis.

III. Results

According to our assessment, the studies used for this review contained a sufficient amount of raw or processed data, making them eligible for inclusion.

Table 1: Comparison of similar study

Study	Sensitivity (%)	Specificity (%)	Positive predictive value(PPV)(%)	Negative predictive value(NPV)(%)	Accuracy (%)
Patil et al [8] (2016)	77.7	84.2	70.0	88.8	82.1
Bamanikar et al(2016)	89.47	88.70	82.92	-	-
Dhakal et al(2016)	77.80	100	100	97	
Atla et al [11] (2015)	94.11	64.28	82.75	85.0	83.3
Joshi et al [12] (2015)	65.38	95.83	94.4	71.8	88.0
Chaudhary et al[13] (2014)	79.37	81.02	65.79	89.52	-
Bindroo et al(2019)	75.24	97.98	96.20	85.38	88.80

Table 2: Shows comparative estimation of NILM cases by different studies.

Study by	Percent of NILM cases
Saha R et al (2005)18	51.16%
Rathore SB et al (2013)16	86%
Selhi PK et al (2013)19	96.08%
Laxmi PV et al (2016)20	67%
Kalyani R et al (2016)17	96.92%
Warpe B.M. et al (2016)	75.14%

Table 3: Shows comparative estimation of IEL's by different studies.

Studies	Percent of IELs in study
Mehmetoglu HC, et al	1.2%
Bal MS, et al (2012)	5%
Warpe B.M. et al (2016)	16.86%
Kalyani R et al (2016)17	3.08%
Rathore SB et al (2013)16	6.6%
Selhi PK et al (2013)19	2.04%

Table 4: Shows the comparative data on ASC-US lesions by different studies.

Study by	Percent of 'ASC-US' cases in study from overall PAP smear cases studied
Saha R et al (2010)18	2.33%
Bal MS et al (2012)22	0.3%
Kalyani R et al (2016)17	1.46%
Selhi PK et al (2013)19	1.6%
Rathore SB et al (2013)16	4%
Warpe B.M. et al (2016)	12.2%

Table 5: Shows the comparative data on ASC-H lesions by different studies

Study by	Percent of 'ASC-H' cases in study from overall PAP smear cases studied
Kalyani R et al (2016)17	0.32%
Warpe B.M. et al (2016)	1.14%

Table 6:Shows the comparative data on 'L-SIL' lesions by different studies

Study by	Percent of 'ASC-US' cases in study from overall PAP smear cases studied
Bal MS et al (2012)22	2.7%
Kalyani R et al (2016)17	0.24%
Laxmi PV et al (2013)20	7.5%
Rathore SB et al (2013)16	1.6%

Warpe B.M. et al (2016)	1.71%

Table 7: Shows the comparative data on 'H-SIL' lesions by different studies

Study by	Percent of 'H-SIL' cases in study from overall PAP smear cases studied
Bal MS et al (2012)22	0.7%
Kalyani R et al (2016)17	0.41%
Laxmi PV et al (2013)20	6%
Rathore SB et al (2013)16	0.4%
Warpe B.M. et al (2016)	1.43%

Table 8: Shows the comparative data on 'SCC' lesions by different studies

Study by	Percent of 'H-SIL' cases in study from overall PAP smear cases studied
Bal MS et al (2012)22	1.3%
Kalyani R et al (2016)17	0.41%
Selhi PK, et al (2013)19	0.16%
Rathore SB et al (2013)16	0.4%
Warpe B.M. et al (2016)	0.29%

IV. Discussion

Cancer is one of the leading causes of death worldwide. Every year about 14 million new cancer cases are detected and 8 million people die from cancer [7]. However, the worldwide distribution of cancer sites varies in different regions. In developing countries like India cervical cancer is a public health problem due to various factors than in the developed countries so much that one-quarter of the worldwide burden of cervical cancers is in India alone [7,8]. It is one of the leading causes of cancer mortality, accounting for 17% of all cancer deaths in women. Other studies show that cervical cancer will occur in approximately 1 in 53 Indian Women compared with 1 in 100women In more developed countries [8]. The cervix is both sentinel for potentially serious genital tract infections and a target for viruses, as well as other carcinogens which may lead to precancerous lesions and invasive carcinoma [9].

The goal of cervical screening is early detection of cervical cancer and precursor lesions. It is stated that the incidence of cervical cancer can be reduced by as much as 80% if the quality, coverage, and follow-up of screening are high. Screening for cancer is known to reduce mortality by early detection and treatment [10, 11]. Unlike other cancer sites, the cervix can be subjected to Screening for early diagnosis and treatment. However, despite the availability of various cervical cancer screening methods, as well as the large burden of disease in India, there is no country wide government-sponsored public health policy on prevention of cervical cancer by either screening or vaccination or both. This Paper is aimed at finding out the efficacy of Pap smear in detecting malignant lesions of the cervix in the preinvasive stage. Most cervical cancers start from an area of the dysplastic epithelium (Transformation zone) which can be detected well by taking a good Pap smear, the best screening program worldwide recommended for sexually active women [12,13,14].

In this paper, the Pap smear examination was compared with histopathological examination the findings of the present study are recapitulated and compared with the results of other studies.This most widely used screening test as of today is simple and acceptable, but it has been found to have false-negative results ranging from 1.1 to

30%, Chhabra et al 2003 (18.7%), Ozkara et al 2002 (5.3%) [15,16]. Variations have been attributed to the difference in cytological expertise, variation in sampling techniques and preparation of the smear. Regarding sampling error and preparation, an artifact like drying artifacts, inadequate fixations, background materials, and thick smears are the most common source of the false negative smears, screening and interpretation mistakes being relatively uncommon [17,18]. Tritz et al found discrepancies between cytologic and histologic diagnoses in 69 out of 615 (11%) patients with a cytologic diagnosis of neoplastic abnormality, source of error may be inappropriate biopsy or faulty biopsy [19]. The small size of the tumor cells and their scarcity in smears are the major sources of false negativity[20]. Adhesion of cells with in the abnormal epithelium is another reason for false negativity. And another important factor is the malignant lesions do not exfoliate at a constant rate. False positivity may be due to removal of the entire lesion by energetic brushing resulting in biopsies with denuded surface or misinterpretation of the cluster of endocervical cells with large nuclei and nucleoli, the cluster of endometrial cells or postmenopausal atrophic cells as abnormal cells.Various studies mentioned the sensitivity and specificity of cytology for detecting cervical neoplasia that ranged from 50-98%[21]. There are different methods that were studied to improve cervical screening, but cervical biopsy has been considered as the gold standard for detecting cervical lesions [15, 16].

The success of screening for cervical cancer is based on the collection of adequate materials and the correct interpretation of abnormal cells. Therefore, better awareness, motivation programs along the use of thin-

Prep Pap liquid-based cytology technique to reduce inadequate sampling errors is recommended for a virtual 100% prevention of cervical cancer in the years to come.

The cervicovaginal smear is considered to be a good method to evaluate the status of uterine cervical epithelium with low cost and easy methodology. Thus, this method has been widely used as a screening test for epithelial neoplasms of the uterine cervix in population-based cancer screening programs and a biannual cervicovaginal smear is recommended for women over the age 30 years by the national cancer screening program [22].The major problem with cervicovaginal smears is the rate of false negative cytology, which has been reported to range between 6 and 55% in several studies [23].

V.   Conclusion

In this study, the screening techniques by PAP smear are significant enough to reduce the incidence of cervical carcinomas, PAP smear test was found to be equally sensitive to histopathological examination for the early detection of different cervical lesions. However, it is advised to perform biopsy if any abnormalities are detected in pap smear for correlation and confirmation.

The study revealed a good correlation between cervical cytology and cervical biopsy. Pap smear is an important screening tool for the detection of precancerous and cancerous lesions of the cervix. It is a less invasive and simple procedure to perform on OPD basis.

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