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Comparative Analysis of Cervical Cytology and Histopathology Findings

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Abstract: Cervical cytology (Pap smear) is a rather popular screening method with variability in the quality of diagnosis quality. Cervical biopsies have been the gold standard in terms of definitive diagnosis using histopathology. This paper sought to evaluate the Pap smear cytology and histopathology diagnosis and to establish how accurate the Pap smear is in diagnosing cervical lesions in a group of 92 patients. A descriptive cross-sectional study was carried out on 92 patients in the different hospitals in Iraq within a 12-month range of the follow-up period that is between June 2023 and June 2024. Sampling of the cervix was done in both traditional (71.74%) and liquid-based (28.26%) cytology samples. The clinical manifestations in the patients were noted, and most frequently, it was irregular vaginal bleeding (40.1%) and vaginal discharge (33.7%). The Pap smear was assessed with regard to histopathological biopsy findings as the benchmarks. In addition, the age group that was affected the most was 40-50 years (41.30%). Cervicitis and CIN I (n=35 and n=34, respectively) were found in histopathological examination, whereas NILM and LSIL (n=34 and n=25, respectively) were found in cytology most commonly. The association of cytology and histology had a significant correlation (P = 0.0001). The Pap smear had a sensitivity of 100% and a specificity of 42.0 in terms of the accuracy of the diagnostic. Positive Predictive Value (PPV) was 18.96, and the Negative Predictive Value (NPV) was 100. Although Pap smear cytology is highly sensitive and has a high predictive value, which is negative, of culling disease, it is also characterized by poor specificity, meaning that it has a high probability of wrongful diagnoses.

Keywords: Cervical Cytology, Histopathological Features, Conventional, and Liquid-Based.

INTRODUCTION

The study of cells is referred to as cytology. It is given the name of Greek cytos that translates to cells. The cells of the cervicovagina are continually developing. The fully grown cells protrude to the surface and are exfoliated. The first exfoliation cells were removed from the posterior fornix, where the cells of the endocervix, ectocervix, and vaginal epithelial cells were present. Hence, it was the exfoliative vaginal cytology. However, it is now scraped directly on the ecto and the endocervix to take the cells. The overall objective is to sample the entire transformation zone (TZ) and also the squamocolumnar junction (SCJ) more. The SCJ is extremely important to the pathogenesis of cervical cancer. Most of the precancerous changes are found in the TZ and at the SCJ. This is why the cell harvesting of this region is extremely critical (Khan, M. S. *et al*., 2005). A Pap smear works based on the principles of identifying morphological abnormalities of exfoliated cervical cells and categorizing them based on a set of standard systems, like the Bethesda System. It is categorized between negative intraepithelial lesions or malignancy (NILM) to high-grade squamous intraepithelial lesions (HSIL) and squamous cell carcinoma (SCC), and gives a guideline to clinical decision-making (Pradhan, B. *et al*., 2007). This has led to a decrease in the incidence and death rates from invasive cancer as a result of early detection and management of preinvasive lesions through cervical cytology. (3) Since 1943, Pap smear cytology has been in use as a screening procedure (Gezer, S. *et al*., 2021). Specificity of standard Pap smear test has been established over the years through a number of studies to be approximately 98-99 moreover sensitivity of Pap smear cytology is 50-75 (Branca, M. *et al*.,) though its false negative yield is also a concern, this is despite the fact that Pap smear cytology is the most viable method to prevent and detect the precancerous conditions of the uterine cervix before it goes invasive. This way, the histologic examination should result in the final diagnosis to determine the accuracy of the cervical cytology. (Smith, B. *et al*., 2016; Kumar, D. *et al*., 2023) Cytology, though the most specific form of screening is today, may not be adequate with premalignant lesions. It is a common practice to assess high-grade epithelial lesions with the help of colposcopy and biopsy. However, the treatment of the low-grade lesions is not clear, and changes were made to this. In some cases, follow-up of pathologic cytology with Pap smear will cause anxiety to patients, and it also precludes following patients who are distant due to their rural location.

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And in such instances, the patients may be occasionally referred to the colposcopy and biopsy. Colposcopy and biopsy can also be used to diagnose high-grade premalignant lesions under cytology (Kothari, S. *et al*., 2014; Abdullah, L. S. 2007; Sachan, P. L. *et al*., 2018). Biopsy and histopathological examination still constitute the gold standard of the diagnosis of the cervical premalignant lesion. The cervical biopsy is an invasive procedure that is being associated with some issues, as it is linked with pain, bleeding, and fibrosis. Therefore, the tendency to work out high-accuracy, suitable non-invasive screening methods in the early diagnosis of cervical premalignant lesions exists. There are reliable and expert physicians and proper technical concerns that affect the accuracy of the Pap smear and the colposcopy (Sinha, R. *et al*., 2020). A number of research studies have compared the diagnostic qualities of these assessments in an attempt to identify the most appropriate screening modality amongst these groups of patients (Kumar, D. *et al*., 2023). However, little data are available on the population of Iraq (Atla B. *et al*., 2015). In the current study, limited studies were assessed and compared the diagnostic accuracy of the pap smear and the colposcopy with the gold standard (cervical biopsy) in the diagnosis of the premalignant lesion of the cervix in Iraqi women in different hospitals in Iraq (Renshaw, A. A. *et al*., 2009; Abali, R. *et al*., 2011).

PATIENTS & METHODS

This cross-sectional study aimed to assess the accuracy of the cervical cytology (Pap smear) diagnosis in the presence of histopathological results of cervical biopsies compared to histopathology. The research group was 92 patients that received both Pap smear screening and colposcopy-guided cervical biopsy at different hospitals in Iraq between June 2023 and June 2024. Medical records and pathology reports contained patient data, such as their age, clinical opening, and cytological/histopathological diagnosis.

Cytological assessment of cervical samples was done through two modalities, namely, traditional Pap smears and liquid-based cytology. All the cytology findings were documented as per the Bethesda System of reporting cervical cytology. The cytological diagnoses include Atypical Glandular Cells (AGC), Atypical Squamous Cells of Undetermined Significance (ASCUS), Atypical Squamous Cells cannot exclude HSIL (ASCH), Low-grade Squamous Intraepithelial Lesion (LSIL), High-grade Squamous Intraepithelial Lesion (HSIL), and Squamous Cell Carcinoma. None of the cases that had no intraepithelial lesions or malignancy were considered as Negative of Intraepithelial Lesion or Malignancy (NILM).

The cervical biopsy tissue histopathological examination was to be used as the ultimate diagnostic standard. The findings of the biopsy were oriented to certain diagnostic categories, such as cervicitis, Cervical Intraepithelial Neoplasia (CIN) I, II, and III, adenocarcinoma, squamous cell carcinoma, etc. Under inclusion and exclusion criteria, this study categorized the patients into inclusion criteria, such as are females between 24 and 74 years of age; females who had a history of vaginal discharge, postcoital bleeding, and irregular vaginal bleeding; females who had a history of cervical erosion, genital warts, and cervical mass. The exclusion criteria were patients who are pregnant women, menstruating women, patients who are not cooperative, and patients who are below 21 years old.

The data were explored, and tables were provided using MS Office Excel 2016 and SPSS software (v. 26). Correlation between nominal data that was tested using Chi-square with p-value <0.05 or less signified that it was significant. The diagnostic performance was evaluated by calculating the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) using a 2x2 contingency table. Pap smard outcomes, which are dichotomized into negative and positive, NILM outcome is negative as compared to ASCUS, LSIL, ASC-H, AGC-favor neoplastic, HSIL, and Squamous cell carcinoma outcome. Sensitivity was expressed as the percentage of true positives (abnormal Pap smear with positive biopsy) of all the positive cases of biopsy, and specificity as a percentage of the true negative cases of the negative cases of the biopsy. The probability of an abnormal versus normal Pap smear as the predictors of the outcome of the biopsy were evaluated in PPV and NPV.

RESULTS

Among the 92 patients that were enrolled in this cohort, most of the samples, totaling 66 samples, are conventional, with a total of 71.74. The rest of 26 samples were categorised as liquid-based, which is 28.26 percent of the patient group.

Most of the patients were of 40 and 50 years of age (40.9 percent), then the age ranges of 30-39 (22.6

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percent) and more than 50 years of age (21.5 percent). The youngest patients (20-29) constituted the least percentage (14.0 percent). Table 2 is in tandem to the age distribution to the cohort under consideration in the histopathology correlation between Pap smear and biopsy outcome.

Also found in the paper indicates that there are 92 patients (clinically) who have gone through Pap smear and cervical biopsy. It shows the distribution of the clinical presentations. Irregular vaginal bleeding was reported by the highest number of 37 patients (40.1%), and then vaginal discharge was reported by 31 patients (33.7%). Cervical erosion occurred in 19 (20.7) patients, and other infrequent manifestations included cervical warts and cervical mass, each in 2 (2.2) patients. The least common clinical feature was dyspareunia, with just 1 found in a patient (1.1%).

Table 1: Classification of types of samples in the 92 patients' cohort.

Types	**Number of patients, [n = 92]**	**Percentage, %**
conventional	66	71.74%
Liquid based	26	28.26%
Total	92	100%
age group		
20 – 29	13	14.13%
30 – 39	21	22.83%
40 – 50	38	41.30%
> 50	20	21.74%
Clinical Feature		
cervical erosion	19	20.7
cervical wart	2	2.2
cervical mass	2	2.2
dyspareunia	1	1.1
Irregular vaginal bleeding	37	40.1
vaginal discharge	31	33.7
Total	92	100

Table 2: Pap smear Correlation to Histopathological Diagnoses.

	Biopsy Results												
Pap Smear Diagnosis	cervical adenocarcinoma	cervicitis	Cervicitis with squamous metaplasia	CIN I	CIN II	CIN III	endocervical polyp	Endocervical tissue and mild	No atypia or malignancy	no ectocervical	Squamous carcinoma	Total	*P*-value
AGC-favor neoplastic	1	0	0	0	0	0	0	0	0	0	0	1	0.0001 (HS)
ASCH	0	0	0	1	1	0	0	0	0	0	0	2	
ASCUS	0	7	0	9	0	0	0	1	2	1	0	20	
HSIL	0	0	0	1	3	2	0	0	1	0	2	9	
LSIL	0	4	0	19	1	0	0	0	1	0	0	25	
NILM	0	24	1	4	0	0	3	0	2	0	0	34	
Squamous cell carcinoma	0	0	0	0	0	0	0	0	0	0	1	1	
Total	1	35	1	34	5	2	3	1	6	1	3	92	

A correlation between the Pap smear diagnosis and the biopsy results showed a statistically significant correlation ($p < 0.001$), Table 4. It is worth noting that high-grade squamous intraepithelial lesion (HSIL) on Pap smear invariably was related to both high-grade cervical intraepithelial neoplasia (CIN II/III) and

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squamous cell carcinoma (SCC) on biopsy, whereas low-grade squamous intraepithelial lesion (LSIL) was mostly associated with CIN I and cervicitis. Atypical squamous cells of undetermined significance (ASCUS) did not reveal a narrow spectrum of histopathological consequences, and, in the majority of the cases, cervicitis and CIN I. Every instance of squamous cell carcinoma, as well as the atypical glandular cells-favor neoplasm on Pap smear were neoplastic on biopsy.

Table 3: Diagnostic Accuracy of Pap Smear Compared to Histopathological Biopsy Results.

p			Biopsy Result		
			Positive	Negative	Total
Pap Smear Result	Positive	Frequency	11	47	58
		% Within biopsy result	100.0%	58.0%	63.0%
	Negative	Frequency	0	34	34
		% Within biopsy result	0.0%	42.0%	37.0%
Total		Frequency	11	81	92
		% Within biopsy result	100.0%	100.0%	100.0%

The Pap smear diagnostic performance versus the gold standard of histopathological biopsy was proved to be highly sensitive (100.0%) and negative predictive value (NPV, 100.0%), which means that a negative Pap smear on cervix health screening is highly effective in the exclusion of significant cervical pathology. Specificity was low, however (42.0%), and the positive predictive value (PPV) was only 19.0%, which were high rate of false- positive results. These results are congruent with the observed distribution, where all the cases that were biopsy confirmed to be positive were also correctly identified using the Pap smear. However, most of the positive Pap smears were associated with negative biopsies. Table 5 shows these findings.

DISCUSSION

The purpose of the study was to determine the test performance (accuracy) of cervical cytology (Pap smear) in the detection of cervical lesions, the gold standard of which are the histopathology results of cervical biopsies (Mitra, A. *et al*., 2017). The demographic information indicated that conventional smears (71.74) and cervical pathology in the age group 40-50 (41.30) would have the highest rate. This age trend agreed with the natural history of cervical carcinogenesis that naturally progresses through HPV infection to precancerous lesions over 10 to 20 years and frequently reaches its highest occurrence during the perimenopausal years. According to the clinical manifestations, irregular vaginal bleeding (40.1) and vaginal discharge (33.7) being the most frequent symptoms, they are similar to the results of the study conducted in the USA and Canada, where opportunistic screening is a usual process, and patients are often referred to the symptomatic rather than detected using the population-wide screening programs (Ratree, S. *et al*., 2019; As, V., & Jain, V. 2010). The Pap smear had a high sensitivity in detecting high-grade lesions. That single case of AGC-favor neoplastic was appropriately linked to a biopsy cervical adenocarcinoma. Moreover, all the cases of HSIL on cytology that were followed with a biopsy demonstrated abnormalities, where 3/9 cases were confirmed CIN II or above. The high level can be considered in this strong association with a p-value of high significance (0.0001). LSIL cytology correlated with CIN I the most (19/25 cases), and also missed 1 case of cervicitis II and oversigned 4 times. On the same note, ASCUS, which is a borderline category, also exhibited a wide spectrum of biopsy findings, including benign cervicitis to CIN I (Asaturova, A. *et al*., 2022). Moreover, the Pap smear showed an ideal positive predictive value of positivity on the biopsy (11/11, 100 percent), that is, all cases predicted to be positive on the cytology were identified to contain some kind of abnormality on the biopsy (Belekar, S. V. *et al*., 2023).

Nevertheless, data demonstrates that there is a serious problem: a high percentage of false positives. Out of 58 cases called as positive by use of cytology, 11 out of them were verified through biopsy, making only

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the specificity of 42.0% (34/81). This is quite contrary to the specificity of modern cytology that is reported to be above 80% in certain studies. When non-NILM results (such as ASCUS, LSIL, etc.) were all that the authors refer to as positive, the phenomenon of low specificity is not surprising. Numerous ASCUS and LSIL findings on cytology are likely to revert or only have benign inflammation on biopsy. The more refined analysis would make calculations more sensitive and specific to high-grade lesions (CIN II+). The sensitivity of a single Pap smear of 50-80% means that 4 true CIN II+ lesions out of 7 were identified (sensitivity of the single Pap smear of HSIL+ ASC-H+ AGC = 47 to 83 percent).

CONCLUSION

The paper establishes that cervical cytology (Pap smear) is a very sensitive screening method that has a high negative predictive value and is effective in excluding compelling cervical pathology, and hence, none of the cases of disease has been missed. It, however, has a low specificity and high positive predictive value, meaning that it gives a high number of false-positive results, especially when it comes to borderline diagnoses such as ASCUS and LSIL. Although a negative Pap smear is very much reliable, positive outcomes, or those that which are of low grade, are often to be confirmed by histopathology through a biopsy to avoid unnecessary anxiety and over-treatment, validating the use of biopsy as the definitive diagnosis standard.

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