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CERVICAL SMEAR IN DUHOK PROVINCE; A PRACTICAL CYTOLOGICAL REVIEW

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ABSTRACT

Background: Cervical smear (also known as Pap smear or Pap test) is a well-known test that saves many women's lives because it helps detect cervical cancerous and precancerous lesions. The objective of this study is to determine the frequency of various cytological abnormalities in women advised to do this test in Duhok Province during 11- year-period (2012 to March 202) since the test was launched. Second, in the same group of women, evaluate the age-specific cytological anomalies. **Method:** A cross-sectional study of 8000 cases from patients visiting Duhok Central Laboratories was conducted from February 2012 to March 2023, while case analysis was achieved within 7-month-period (June 2023 to February 2024). The Pap test performed included liquid-based cytology samples collected by pathologists, gynecologists and well-trained technicians on women visiting hospitals for various complaints. Data, including age groups and pathological diagnoses, were extracted from electronic patient files and analyzed following ethical approval from the Human Research Ethics Committee at Duhok University/College of Medicine. **Results:** In the studied samples, 95.2% were diagnosed as Negative for Intraepithelial Lesions or malignancy (NILM) with the highest rate (98.3%) in patients aged ≤20 years and the lowest (92.5%) in those aged 51-60 years. Atypical Squamous cells of Undetermined Significance (ASCUS) was found in 4%, with the highest rate (5.5%) in patients aged 51-60 years. Other diagnoses such as Atypical Squamous cells, High Squamous intraepithelial Lesion cannot be excluded (ASC-H), Atypical Glandular cells of Undetermined Significance AGUS), Low Squamous intraepithelial Lesion (LSIL), High Squamous intraepithelial Lesion (HSIL), invasive Squamous Cell Carcinoma (SCC), and adenocarcinoma were rare, with rates below 0.3% and no significant differences between age groups except for AGUS ($p = 0.001$) and adenocarcinoma ($p = 0.032$). **Conclusion:** The distribution of cervical cytological abnormalities in the study matches previous researches performed in the same locality and elsewhere in the world. Cytologically, yielding precancerous and cancerous cases among different age groups especially young women in this study worthens application of Pap smear screening program in this locality and necessitates testing and vaccination for HPV infection among young women to prevent, detect and early treat HPV-related cervical epithelial abnormalities.

KEYWORDS: Cervical, smear, A practical, cytological, review.

INTRODUCTION

Cervical cancer remains one of the most significant health issues affecting women globally, despite being highly preventable through early detection and appropriate intervention. The primary method for early detection of cervical cancer and its precursors is the cervical smear test, also known as the Pap smear or Pap test. The technique of this test, introduced by Dr. George Papanicolaou in the 1940s, has drastically reduced the incidence and mortality rates associated with cervical cancer.[1] Cervical smear test is achieved by collection of cells from uterine cervix, which are then examined microscopically for any cellular abnormalities. These abnormalities can range from benign cellular changes to high-grade lesions that indicate a potential progression to cervical cancer to invasive cancer.[2] The effectiveness of cervical smearing in detecting early-stage cervical cancer and pre-cancerous changes hinges on the quality of the technique and cytological review process which involves a careful examination of the collected samples by trained

cytotechnologists, gynecologist, and pathologists who identify and classify cellular abnormalities based on established criteria. The practical cytological review of cervical smears is critical in regions with high cervical cancer, where robust screening programs can significantly reduce the disease burden. The World Health Organization (WHO) emphasizes the importance of organized screening programs and the role of cytology in detecting Cervical Intraepithelial Neoplasia (CIN) and invasive cervical cancer (CA) at early stages.[3] Several factors influence efficacy of Pap smear. These include sample collection techniques, the quality of the cytological examination and the interpretative skills of the cytologists. Sample collection must be performed meticulously to ensure adequate cellular material obtained from transformation zone of cervix, where most precancerous and cancerous lesions originate.[4] Conventional Pap smear is the first applied technique introduced, and many centers still apply this method in cervical sampling, while Liquid-Based Cytology (LBC) has been introduced as an improvement over conventional Pap smears, providing better sample preservation and reducing the likelihood of unsatisfactory samples.[5] The cytologic review process involves microscopic examination of the Pap-stained cervical cells. Pathologists use various classification systems to report the cytological findings, with the Bethesda System being the most widely adopted. This system categorizes cervical cytology results into several categories, including Negative for Intraepithelial Lesions or malignancy (NILM), Atypical Squamous cells of Undetermined Significance (ASCUS), Low Squamous intraepithelial Lesion (LSIL), High Squamous intraepithelial Lesion (HSIL), and more. Accurate interpretation requires extensive training and experience, as well as adherence to quality assurance protocols.[2] In Duhok, Iraq, the implementation of Pap smears has been introduced for detection of precancerous and early cancerous cervical epithelial abnormalities since 2004. The objective of this study is to determine the frequency of various cytological abnormalities in women who attempted cervical smearing in the Duhok Province. Second, in the same group of women, evaluate the age-specific cytological anomalies.

METHOD

This cross-sectional study analyzed 8000 cases from patients visiting Duhok Central Laboratories during 11-year-period (from February 2012 to March 2023). The study was conducted within 7-month-period (between June 2023 and February 2024). Patient information included age groups. Patients were presented with various complaints (such as vaginal discharge, foul vaginal odor, post-coital vaginal bleeding and pelvic pain. The technique applied was ThinPrep-LBC. Using special devices, the materials have been taken from uterine cervix by gynecologists, pathologists and well-trained cytotechnologists. The used devices were broken and rinsed in vials containing methanol-based preservative liquid, and then sent for cytopathological review to the Pathology Department in the Central Laboratories in Duhok within two days of collection. Using automated processor, the collected materials were filtered to remove debris, blood and mucus, and then pressed on special slides labeled with numbers according to the applied laboratory protocols. Slides were assigned microscopically by pathologists. Data extraction involved a specially designed data sheet encompassing demographic data and Pap smear results. Cervical smear results were classified according to the Bethesda System. The study was approved by the Human Research Ethics Committee at the College of Medicine, University of Duhok. Statistical analysis was conducted using SPSS version 22. For categorical data, frequency and percentage were utilized. The Chi-square test was employed to assess associations between variables, and Pearson correlation was used to examine the relationships between continuous variables. A p-value of 0.05 or less was considered statistically significant.

RESULTS

As shown in table 1, more than 90% of women were between 21 years and 50 years of age; 37.8% at age group 31-40 years old and 29.6% at age group 21-30 years old while 23.8% at age group 41-50 years old. Cytologically, 95.2% of cases were NILM. Only 4 cases were diagnosed as malignant (3 SCC and 1 adenocarcinoma) and 23 squamous intraepithelial lesions (18 LSIL, 5 HSIL). The remainders were addressed as unknown significance; these included 321 (4%) ASCUS, 0.3 AGUS, 0.1 ASCH).

Table 1: Distribution of patients according to age groups (years) and pathological diagnosis.

Variables		Frequency	Percentage
	≤20	124	1.6
Age groups (years)	***21-30***	2365	29.6
	31-40	3020	37.8
	41-50	1906	23.8
	51-60	452	5.7
	>60	133	1.7
Cytological	***NILM***	7625	95.2
Diagnosis	***ASCUS***	321	4.0
	AGUS	23	0.3
	ASCH	4	0.1
	LSIL	18	0.2
	HSIL	5	0.1
	CA SCC	3	0.075
	Adeno CA	1	0.025
Total		**8000**	**100.0**

**NILM (Negative for Intraepithelial Lesion or Malignancy), ASCH (Atypical Squamous Cells, Cannot Exclude HSIL), SCUS (Atypical Squamous Cells of Undetermined Significance), AGUS (Atypical Glandular Cells of Undetermined Significance), LSIL (Low-Grade Squamous Intraepithelial Lesion), HSIL (High-Grade Squamous Intraepithelial Lesion), CA*

SCC (Carcinoma Squamous Cell Carcinoma), Adeno CA (Adenocarcinoma).

As presented in Table 2, the highest rates of NILM (35.9%) and ASCUS (1.6%) cases were among patients 31-40 years age group. The differences were significant ($p < 0.001$and 0.01 respectively). Most cases of LSIL and all HSIL were between 21 and 50 years. Two patients with SCC felled between 41 and 50 years and 1 within 31-40 years age intervals. The single patient with adenocarcinoma was 69 years old.

Table 2: association between age groups and pathological diagnosis.

	Age (years)							
	≤20	**21-30**	**31-40**	**41-50**	**51-60**	**> 60**	**Total**	
Diagnosis	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)†**	**p**
NILM	119 (1.5)	2289 (28.6)	2874 (35.9)	1797 (22.5)	419 (5.2)	127 (1.6)	7625 (95.5)	**< 0.001***
ASCUS	2 (0.02)	69 (0.9)	130 (1.6)	90 (1.1)	25 (0.3)	5 (0.06)	321 (4.0)	**0.011***
AGUS	0 (0.0)	1 (0.01)	7 (0.09)	9 (0.1)	6 (0.07)	0 (0.0)	23 (0.3)	**0.001****
ASC-H	0 (0.0)	0 (0.0)	1 (0.01)	1 (0.01)	2 (0.02)	0 (0.0)	4 (0.1)	0.058**
LSIL	0 (0.0)	5 (0.06)	6 (0.07)	6 (0.07)	1 (0.01)	0 (0.0)	18 (0.2)	0.908**
HSIL	0 (0.0)	1 (0.01)	1 (0.01)	3 (0.03)	0 (0.0)	0 (0.0)	5 (0.1)	0.512**
CA SCC	0 (0.0)	0 (0.0)	1 (0.01)	2 (0.02)	0 (0.0)	0 (0.0)	3 (0.0)	0.513**
Adeno CA	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.01))	1 (0.0)	**0.032****
Total	121 (1.52)	2365 (29.6)	3020 (37.7)	1908 (23.8)	453 (5.6)	133 (1.7)	8000 (100.0)	

*By Chi square test. **By Fisher's exact test. †Note that the percentages in the table were rounded to the nearest number.

DISCUSSION

The findings presented in the study provide a variable degree of cervical cytological abnormalities with variable distribution across different age groups. This discussion analyzes these results in the context of existing literature, highlighting agreements and possible explanations for the observed patterns. The study indicates that majority of patients (95.2%) were diagnosed as Negative for Intraepithelial Lesion or Malignancy (NILM). This high prevalence of NILM is consistent with findings from other studies. For instance, research conducted by Wang J et al. (2020) in Sweden showed that most women undergoing cervical screening have normal cytological findings. This trend underscores the effectiveness of routine cervical screening programs in identifying and ruling out malignant changes in a significant proportion of the population.[8] The age-specific prevalence rates observed in the study also align with global data. The highest rate of NILM and ASCUS patients were found in patients 31-40 years of ages, most LSIL and all HSIL patients were between 21 and 50 years while 2 out of 3 patients with SCC were between 41 and 50 years and the single woman with adenocarcinoma was above 60 years. This decline in NILM and ASCUS prevalence with increased dysplastic and malignant cases with increasing age form a common finding. According to a study by Moscicki AB et al. (2020), the prevalence of high-risk human papillomavirus (HPV) infections, which are associated with cervical abnormalities, increases with age, peaking in women aged 30-39 years and then declining. This pattern explains the lower NILM rates and higher ASCUS rates in older age groups, as seen in the current study.[9] A diverse distribution of different cytological findings has been reported. Lee MH et al. (2018), who reported a higher prevalence of ASCUS in older women. The increased prevalence in the older age group could be attributed to the cumulative exposure to HPV and other risk factors over time, which may lead to cellular changes detectable by cytological screening.[10] The study also reported rare occurrences of other diagnoses such as ASC-H, AGUS, LSIL, HSIL, and CA SCC, with rates of 0.1%, 0.3%, 0.2%, 0.1%, and almost 0%, respectively. These findings are in line with the low prevalence rates of high-grade lesions and cervical cancers observed in other studies. For example, the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program data shows that the incidence of cervical cancer is relatively low, particularly in populations with regular screening practices.[11] The study's finding that AGUS was most prevalent among those aged 41-60 years and absent in those aged ≤20 years and >60 years is consistent with the understanding that glandular cell abnormalities are more common in middle-aged women. According to Marinova P et al. (2010), AGUS is often associated with underlying significant pathology, and its prevalence is higher in women aged 40-60 years.[12] Regarding LSIL, HSIL, and CA SCC, the low rates (0.2%, 0.1%, and almost 0%, respectively) observed in the study reflect its effectiveness in early detection and intervention strategies of precancerous neoplastic lesions. The age-specific prevalence rates of precancerous and cancerous cervical lesions observed reflect the natural history of HPV infection and cervical disease progression. As well, the low prevalence of cancerous lesions in this study may indicate their low rates among women living in this specific locality probably because of the social and religious impact on women habits. The singular case of adenocarcinoma in a patient aged >60 years highlights the rarity of this type of cervical cancer in this region. This finding is supported by studies like those by Gravdal BH et al. (2021), which note that adenocarcinoma is less common than squamous cell

carcinoma but tends to be more aggressive and often diagnosed at a later stage.[13]

The strengthens of the present study lies in the facts that the study findings on the distribution of cervical cytological abnormalities align with existing literature, demonstrating the crucial role of cervical smearing in detecting precancerous and early cancerous lesions among young and reproductive aged women to prevent their progression to the life-threatening, ominous advanced cervical cancer.

CONCLUSION

The distribution of cervical cytological abnormalities in the study matches previous researches performed in the same locality and elsewhere in the world. Cytologically, yielding precancerous and cancerous cases among different age groups especially young women in this study underscores the importance of applying regular Pap smear screening to ensure early detection and life-saving intervention and necessitates testing and vaccination for HPV infection among young women.

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