



Cervical Cytological Findings among Women Attending a Tertiary Care Hospital in Sana'a, Yemen

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ABSTRACT

Objective: To determine the frequency and pattern of abnormal cervical smear findings among women attending the University of Science and Technology Hospital (USTH) in Sana'a city.

Methods: This study is a retrospective, cross-sectional study. Records of women examined by conventional Pap smears in the Histopathology Laboratory of USTH over a 4-year period (from January 2013 to December 2016) were retrieved and analyzed for abnormalities according to the Bethesda system.

Results: Of 688 cases, 599 with satisfactory records were analyzed. The mean age of the cases was 39.18±10.23 years (range: 19–75). Epithelial cell abnormalities (ECAs) were found in 47 cases (7.8%), and these were categorized as follows: ASCUS in 4.5% (27/599) of cases followed by atypical glandular cells (AGC) (2.2%; 13/599) and LSIL (0.5%; 3/599), while ASCH and HSIL abnormalities were equally observed among 0.3% (2/599 each) of cases. Of patients positive Pap smear findings, ASCUS was the most frequent type of ECA (57.4%; 27/47) followed by AGC (27.7%; 13/47) and LSIL (6.4%; 3/47), while ASCH and HSIL were the least frequent ECAs among Yemeni patients. ECAs were significantly more prevalent among women aged >40 years (10.8%) compared with those aged <40 years (5.5%).

Conclusions: Cervical cytological abnormalities are not uncommon among women in Yemen, where the AGC is frequent among about a third of women with abnormal Pap smear findings and affects women of different ages. This requires more attention and training of doctors to master good sample taking, preparation and diagnosis with a focus on glandular changes.

Keywords: Cervical cytology, Pap smear, ECA, AGC, Yemen

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1. Introduction

Cervical cancer is considered as the fourth leading cause of female cancers worldwide. More than 528,000 new cases were estimated in 2012, of which about 86% occurred in the least developed countries. Moreover, approximately 266,000 females died of cervical cancer, representing 7.5% of all female cancer deaths (1). In developing countries, cervical cancer is the second most frequently diagnosed cancer after breast cancer and the third leading cause of cancer death after breast and lung cancers (1). Its highest incidence rates are in Eastern Africa, while its lowest rates are in Western Asia (1). Such a variation may reflect differences in predisposing risk factors, prevalence of human papillomavirus (HPV) infection as well as the use of screening and diagnostic methods (1–3).

Infection with HPV is the main risk factor for cervical cancer, which is believed to have a causal role in all of cervical cancer cases (4). Although more than a hundred HPV types have been identified, only some types can cause cervical cancer. HPV 16 and 18 are the most common subtypes identified in cervical cancer, where they account for about 70% of cervical cancers worldwide (5). Nevertheless, cervical cancer is preventable if precancerous lesions are diagnosed early by Pap smear screening and subsequently treated. Pap smear screening remains an effective and widely used method for early detection of pre-cancer and cervical cancer. This test may also detect infections and abnormalities in the endocervix and endometrium (6).

Cervical cancer is more common among women not undergoing regular cervical cytological tests. Squamous cell carcinoma was 3.9 and 13 times more in women screened once every three and ten years, respectively, compared with those screened annually (7).

In Yemen, 8.5 million women aged 15 years or older are at risk of developing cervical cancer. It is estimated that 198 women are diagnosed with cervical cancer and 117 die from the disease each year. Cervical cancer in the country ranks as the ninth most frequent cancer among women and the tenth most frequent cancer among women aged 15–44 years (8). However, there is no effective cervical screening program for early detection of invasive cervical neoplasia and for starting appropriate management to reduce female mortality rates due to cervical cancer. This plays a risky role in the prognosis of cervical cancer.

Data on the cervical cytological abnormalities in Yemen are not available (9). Therefore, this study is the first to report on abnormal cervical Pap smear findings among Yemeni women. It aimed to determine the frequency and pattern of abnormal cervical smear findings in relation to age among women attending the University of Science and Technology Hospital (USTH), a tertiary care hospital based at Sana'a, Yemen.

2. Methods

2.1 Study design and categorization of smear findings

This study is a retrospective, cross-sectional study. Records of women examined by conventional Pap smears in the Histopathology Laboratory of the USTH over a 4-year period (from January 2013 to December 2016) were retrieved and analyzed for abnormalities according to The Bethesda System (TBS) (10).

Unsatisfactory cytology reports were excluded. The included smears were those with very few epithelial cells or where the morphology of the cells was obscured by blood or severe inflammation according to the guidelines of TBS



(10). The following categories were used: negative for intraepithelial lesions or malignancy (NILM), atypical squamous cells of undetermined significance (ASCUS), ASCUS results with possible HSIL (ASC-H), low-grade squamous intraepithelial lesions (LSILs), high-grade squamous intraepithelial lesions (HSILs) and atypical glandular cells (AGCs) and carcinomas.

2.2. Statistical analysis

Data were analyzed using the IBM SPSS Statistics, version 21.0 (IBM Corp., Chicago, IL, USA). Descriptive statistics were presented as frequencies, percentages or means \pm standard deviations. Chi-square test was used to determine significant differences between the proportions of age groups, where two-tailed *P* value <0.05 was considered statistically significant.

3. Results

Of 688 cases, 599 satisfactory cases (87%) were analyzed and 89 cases (13 %) with unsatisfactory reports were excluded. The average age of the 599 satisfactory cases was 39.2 ± 10.2 , ranging from 19 to 75 years. However, the age of cases with epithelial cell abnormalities was between 22 and 71 years, with the mean age being $43.11 \text{ years} \pm 11.12$. As shown in Table (1), the majority of women screened by Pap smear for cervical cancer were in the age group of 30–39 years, followed by those belonging to the 40–49 age groups, while those aged ≥ 60 years were the least frequent.

Table (2) shows that the epithelial cell abnormalities (ECAs) were found in 7.8% (47/599) of cases, which were distributed as follows: ASCUS in 4.5% (27/599) of cases followed by AGC (2.2; 13/599) and LSIL (0.5%; 3/599). However, ASCH and HSIL abnormalities were equally observed among 0.3% (2/599) of cases each. On the other hand, Figure (1)

shows that ASCUS was the most frequent type of ECAs (57.4%/ 27/47) followed by AGC (27.7%; 13/47) and LSIL (6.4%; 3/47), while ASCH and HSIL were the least frequent ECAs among Yemeni patients.

Table 1. Age distribution of women undergoing Pap smear screening in the USTH in Sana'a in the period 2012–2016

Age category	n (%)
<30	113 (18.9)
30–39	217 (36.2)
40–49	160 (26.7)
50–59	97 (16.2)
≥ 60	12 (2.0)
Total	599 (100)

ASCUS, abnormal squamous cells of undetermined significance; ASCH, abnormal squamous cells-high grade cannot be excluded; LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion; AGC, atypical glandular cells.

Table 2. Frequency of epithelial cell abnormalities using the revised Bethesda system among the study population (N=599)

Epithelial cell abnormalities	n (%)	Mean age (years)
ASCUS	27 (4.5)	42 ± 13.3
ASCH	2 (0.3)	48 ± 1.4
HSIL	2 (0.3)	45 ± 0.0
LSIL	3 (0.5)	45 ± 8.7
AGC	13(2.2)	43.9 ± 8.4
Total	47 (7.8)	43.1 ± 11.1

ASCUS, abnormal squamous cells of undetermined significance; ASCH, abnormal squamous cells-high grade cannot be excluded; LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion; AGC, atypical glandular cells.

Table (3) shows that ECAs were more prevalent among women aged ≥ 40 years (10.8%) compared to those < 40 years (5.5%), with a statistically significant difference ($\chi^2 = 5.81$, $P = 0.016$). However, there was no statistically significant difference for AGC according to age ($\chi^2 = 1.49$, $P = 0.22$).



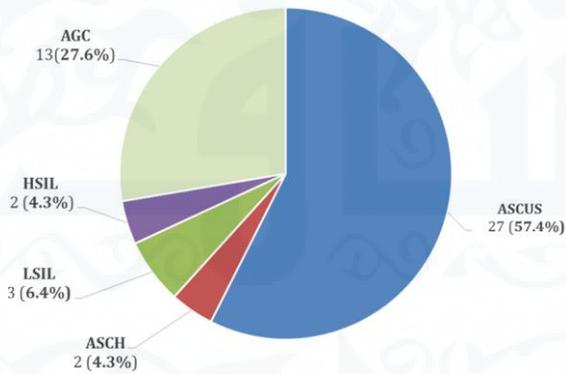


Figure 1. Pattern of Epithelial cell abnormalities among women attending a tertiary health care hospital in Sana'a city (2012-2016)

Table 3. Comparison of epithelial cell abnormalities and atypical glandular cells among women with abnormal Pap smear findings in Sana'a according to age

Age group	N	Type of abnormalities			
		ECA		AGC	
		n (%)	χ^2 (P value)	n (%)	χ^2 (P value)
<40	330	18 (5.5)	5.81	5 (1.5)	1.49
≥40	269	29 (10.8)	(0.016*)	8 (3.0)	(0.220)
Total	599	47 (7.8)		13 (2.2)	

ECA, epithelial cell abnormalities; AGC, atypical glandular cells; * statistically significant at $P < 0.05$.

4. Discussion

The overall frequency of ECAs among Yemeni women based on TBS classification of Pap smear findings in our study was 7.8%. This result is relatively higher than those found in many Arab countries including the UAE (11, 12), Kuwait (13), some regions of Saudi Arabia (14-16), Alexandria, Egypt (17) and Jordan (18). However, it is very close to those reported from south-western Saudi Arabia (7.9%) (19) and Egypt (7.8%) (20). On the other hand, it is lower than those reported by some studies from Iraq (19.7%) (21), western Saudi Arabia (17.3%) (22) and Nablus, Palestine (11.9%) (23).

The significantly higher prevalence of ECA among women aged 40 years and older in

our study is in agreement with previous studies that found a relationship between age and ECA (24, 25).

In the present study, ASCUS was the most prevalent ECA type (57.4%), and this is in accordance with the findings of many other studies in Arab (11-13, 18-20, 23) and non-Arab countries (24, 26-29) On the other hand, the current study revealed that AGCs are not uncommon in Yemeni women since they represent about one-third of all ECAs among studied women. This finding is consistent with the majority of studies in the Arab region (13, 18-23). Moreover, because cytology-based screening has a relatively lower sensitivity for the detection of early glandular lesions than for the squamous-cell cancer precursors (30), the prevalence rate of AGC is expected to be higher than what was found in our study.

The high prevalence of AGC in our study requires attention and further studies because of its clinical importance as the percentage of cases associated with an underlying high-grade disease is higher than for ASCUS (10). According to follow-up studies, high-grade lesions (either squamous or glandular) may be seen in 10-39% of such cases (10).

On comparing the results of several studies from Arab countries (13, 18-23), including those of the present study, with those from non-Arab countries (24-27), the frequency of AGC is much higher in the Arab countries. This, in turn, requires more emphasis, further studies and follow-up.

In a study on the trend of the cellular changes during a period of 21 years (between 1992 and 2012) in Kuwait, Kapila et al. (13) noted a significant increase in the number of glandular changes. On the other hand, a recent study in



Saudi Arabia stressed the need to focus more on glandular abnormalities (15).

Several studies reported increasing rates of adenocarcinoma among younger women, particularly under the age of 40 (31–35). This is in accordance with the finding of the present study that AGC affects both of women younger than 40 years and older. However, there was no statistically significant difference according to age.

Regarding the HSIL that has emerged as the central purpose of cervical cytology screening (10), the frequency in the present study was 0.3%. This frequency is one of the lowest frequencies in the Arab region and the world. In Arab countries, it was 5% in Iraq (21), 1.0% in Kuwait (13), 0.7–0.9% in Saudi Arabia (14, 16, 19, 22), and 0.8% in the United Arab Emirates (11, 12). However, in non-Arab countries, it was 1.8% in Bangladesh (25) and 1.9% in South Africa (27). Since HSIL is associated with HPV persistence and higher risk for progression (10), the low prevalence of HSIL in our study may suggest that the existence of squamous lesions caused by HPV is not common in our population.

This study is limited by being hospital-based among women referred for screening based on a gynecological indication. Therefore, the results may not reflect the true estimates of abnormal cytological findings among Yemeni women in all parts of the country.

5. Conclusions

Cytological cervical abnormalities are relatively common among women in Yemen. The AGCs are more prevalent than squamous intraepithelial lesions, affecting women of different ages. This requires more attention and training of physicians to master good sampling, preparation and diagnosis with a focus on glandular changes.

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Authors' contributions

MA & AS conceptualized the idea and collected the data of the study. AAA designed the study and analyzed and interpreted the collected data of the study. AAA & AS wrote the initial discussion, and MA drafted the initial version of the manuscript. All authors read, revised and approved the final draft of the manuscript.

Competing interests

The authors declare that they have no competing interests associated with this article.

Ethical approval

This study was approved by the Research Ethics Committee of the Faculty of Medicine and Health Sciences, University of Science and Technology, Sana'a, Yemen. Patients' data retrieved from records were dealt with anonymously.

References

1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer* 2015; 136: E359–86. [PubMed](#) • [DOI](#) • [Google Scholar](#)
2. Bruni L, Diaz M, Castellsagué M, Ferrer E, Bosch FX, de Sanjosé S. Cervical human papillomavirus prevalence in 5 continents: meta-analysis of 1 million women with normal cytological findings. *J Infect Dis* 2010; 202: 1789–99. [PubMed](#) • [DOI](#) • [Google Scholar](#)
3. Vaccarella S, Lortet-Tieulent J, Plummer M, Franceschi S, Bray F. Worldwide trends in cervical cancer incidence: impact of screening against changes in disease risk factors. *Eur J Cancer* 2013; 49: 3262–73. [PubMed](#) • [DOI](#) • [Google Scholar](#)
4. Villain P, Gonzalez P, Almonte M, Franceschi S, Dillner J, Anttila A, et al. European code against cancer 4th edition: infections and cancer. *Cancer Epidemiol* 2015; 39: S120–38. [PubMed](#) • [DOI](#) • [Google Scholar](#)
5. Al-Jaroudi D, Hussain TZ. Prevalence of abnormal cervical cytology among subfertile Saudi women. *Ann Saudi Med* 2010; 30: 397–400. [PubMed](#) • [DOI](#) • [Google Scholar](#)
6. Saslow D, Solomon D, Lawson HW, Killackey M, Kulasingam SL, Cain J, et al. American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology



- screening guidelines for the prevention and early detection of cervical cancer. *Am J Clin Pathol* 2012; 62: 147–72. [PubMed](#) • [DOI](#) • [Google Scholar](#)
7. Kuo DY, Goldberg GL. Screening of cervical cancer: where do we go from here? *Cancer Invest* 2003; 21: 157–61. [PubMed](#) • [DOI](#) • [Google Scholar](#)
 8. Bruni L, Barrionuevo-Rosas L, Albero G, Serrano B, Mena M, Gómez D, et al. ICO Information Centre on HPV and Cancer (HPV Information Centre). Human papillomavirus and related diseases in the world. Summary Report 27 July 2017 [cited 29 May 2018]. Available from: <http://www.hpvcentre.net/statistics/reports/XWX.pdf>
 9. Abdul-Aziz M. Knowledge, attitude and practice towards cervical cancer among reproductive health clients at the University of Science & Technology Hospital - Sana'a in Yemen. *Yemeni J Med Sci* 2012; 6. [Google Scholar](#)
 10. Solomon D, Davey D, Kurman R, Moriarty A, O'Connor D, Prey M, et al. The 2001 Bethesda System: terminology for reporting results of cervical cytology. *JAMA* 2002; 287: 2114–9. [PubMed](#) • [DOI](#) • [Google Scholar](#)
 11. Ghazal-Aswad S, Gargash H, Badrinath P, Al-Sharhan MA, Sidky I, Osman N, et al. Cervical smear abnormalities in the United Arab Emirates: a pilot study in the Arabian Gulf. *Acta Cytol* 2006; 50: 41–7. [PubMed](#) • [DOI](#) • [Google Scholar](#)
 12. Al Zaabi M, Al Muqbali S, Al Sayadi T, Al Ameer S, Coetsee K, Balayah Z, et al. Age specific cytological abnormalities in women screened for cervical cancer in the Emirate of Abu Dhabi. *Asian Pac J Cancer Prev* 2015; 16: 6375–9. [PubMed](#) • [Google Scholar](#)
 13. Kapila K, Sharma PN, George SS, Al-Shaheen A, Al-Juwaiser A, Al-Awadhi R. Trends in epithelial cell abnormalities observed on cervical smears over a 21-year period in a tertiary care hospital in Kuwait. *Sultan Qaboos Univ Med J* 2015; 15: e112–5. [PubMed](#) • [Google Scholar](#)
 14. Jamal A, Al-Maghrabi JA. Profile of Pap smear cytology in the western region of Saudi Arabia. *Saudi Med J* 2003; 24: 1225–9. [PubMed](#) • [Google Scholar](#)
 15. Nasser H, AlAyaf M, Atallah A, Aminulislam M, Rizwan L, Aodah A, et al. Eleven-year review of data on Pap smears in Saudi Arabia: We need more focus on glandular abnormalities! *Ann Saudi Med* 2017; 37: 265–71. [PubMed](#) • [DOI](#) • [Google Scholar](#)
 16. Balaha MH, Al Moghannum MS, Al Ghwinem N, Al Omran S. Cytological pattern of cervical Papanicolaou smear in eastern region of Saudi Arabia. *J Cytol* 2011; 28: 173–7. [PubMed](#) • [DOI](#) • [Google Scholar](#)
 17. Abdel-Hadi M, Khalaf A, Aboukassam H, Naeem N, Baqy MA, Sallam H. Cervical intraepithelial lesions in females attending Women's Health Clinics in Alexandria, Egypt. *CytoJournal* 2015; 12: 13. [PubMed](#) • [DOI](#) • [Google Scholar](#)
 18. Maraqa B, Lataifeh I, Otay L, Badran O, Nouri YQ, Issam I, et al. Prevalence of abnormal Pap smears: a descriptive study from a cancer center in a low-prevalence community. *Asian Pac J Cancer Prev* 2017; 18: 3117–21. [PubMed](#) • [DOI](#) • [Google Scholar](#)
 19. Elhakeem HA, Al-Ghamdi AS, Al-Maghrabi JA. Cytopathological pattern of cervical Pap smear according to the Bethesda system in Southwestern Saudi Arabia. *Saudi Med J* 2005; 26: 588–92. [PubMed](#) • [Google Scholar](#)
 20. El All HS, Refaat A, Dandash K. Prevalence of cervical neoplastic lesions and human papillomavirus infection in Egypt: National Cervical Cancer Screening Project. *Infect Agent Cancer* 2007; 2: 12. [PubMed](#) • [DOI](#) • [Google Scholar](#)
 21. Chkhaim TJ, Ali HH, Mosa LR, Abdalghafour KH. Cervicovaginal smears' classification using the Bethesda System (TBS) 2001: a cytopathological study. *Iraqi J Med Sci* 2013; 11: 250–7. [Google Scholar](#)
 22. Altaf FJ, Mufti ST. Pattern of cervical smear abnormalities using the revised Bethesda system in a tertiary care hospital in western Saudi Arabia. *Saudi Med J* 2012; 33: 634–9. [PubMed](#) • [Google Scholar](#)
 23. Musmar SG. Pattern and factors affecting pap smear tests in Nablus: a retrospective study. *Middle East J Fam Med* 2004; 2: 7–12. [Google Scholar](#)
 24. Arbyn M, Van Nieuwenhuysse A, Bogers J, De Jonge E, De Beeck LO, Matheï C, et al. Cytological screening for cervical cancer in the province of Limburg, Belgium. *Eur J Cancer Prev* 2011; 20: 18–24. [PubMed](#) • [DOI](#) • [Google Scholar](#)
 25. Banik U, Bhattacharjee P, Ahamad SU, Rahman Z. Pattern of epithelial cell abnormality in Pap smear: a clinicopathological and demographic correlation. *CytoJournal* 2011; 8: 8. [PubMed](#) • [DOI](#) • [Google Scholar](#)
 26. Insinga RP, Glass AG, Rush BB. Diagnoses and outcomes in cervical cancer screening: a population-based study. *Am J Obstet Gynecol* 2004; 191: 105–13. [PubMed](#) • [DOI](#) • [Google Scholar](#)
 27. Fonn S, Bloch B, Mabina M, Carpenter S, Cronje H, Maise C, et al. Prevalence of pre-cancerous lesions and cervical cancer in South Africa—a multicentre study. *S Afr Med J* 2002; 92: 148–56. [PubMed](#) • [Google Scholar](#)
 28. Massad LS, Einstein MH, Huh WK, Katki HA, Kinney WK, Schiffman M, et al. 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. *Obstet Gynecol J Low Genit Tract Dis* 2013; 17: S1–27. [PubMed](#) • [DOI](#) • [Google Scholar](#)
 29. Campos NG, Castle PE, Schiffman M, Kim JJ. Policy implications of adjusting randomized trial data for economic evaluations: a demonstration from the ASCUS-LSIL Triage Study. *Med Decis Making* 2012; 32: 400–27. [PubMed](#) • [DOI](#) • [Google Scholar](#)
 30. Bosch FX, De Sanjosé S. Chapter 1: Human papillomavirus and cervical cancer—burden and assessment of causality. *J Natl Cancer Inst Monogr* 2003; 31: 3–13. [PubMed](#) • [DOI](#) • [Google Scholar](#)



31. Bray F, Carstensen B, Møller H, Zappa M, Žakelj MP, Lawrence G, et al. Incidence trends of adenocarcinoma of the cervix in 13 European countries. *Cancer Epidemiol Biomarkers Prev* 2005; 14: 2191–9. [PubMed](#) • [DOI](#) • [Google Scholar](#)
32. Horst J, Siebers AG, Bulten J, Massuger LF, Kok IM. Increasing incidence of invasive and in situ cervical adenocarcinoma in the Netherlands during 2004–2013. *Cancer Med* 2017; 6: 416–23. [PubMed](#) • [DOI](#) • [Google Scholar](#)
33. Smith HO, Tiffany MF, Qualls CR, Key CR. The rising incidence of adenocarcinoma relative to squamous cell carcinoma of the uterine cervix in the United States--a 24-year population-based study. *Gynecol Oncol* 2000; 78: 97–105. [PubMed](#) • [DOI](#) • [Google Scholar](#)
34. Liu S, Semenciw R, Mao Y. Cervical cancer: the increasing incidence of adenocarcinoma and adenosquamous carcinoma in younger women. *CMAJ* 2001; 164: 1151–2. [PubMed](#) • [Google Scholar](#)
35. Oh CM, Jung KW, Won YJ, Shin A, Kong HJ, Jun JK, et al. Trends in the incidence of in situ and invasive cervical cancer by age group and histological type in Korea from 1993 to 2009. *PLoS One* 2013; 8: e72012. [PubMed](#) • [DOI](#) • [Google Scholar](#)

