FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 02 ISSUE 01 Pages: 1-8
SJIF IMPACT FACTOR (2021: 5.14)
OCLC – 1272874727 METADATA IF – 6.986
Publisher: Frontline Journals

Journal Website: https://frontlinejournals.org/journals/index.php/fmspj

Research Article

EPIDEMIOLOGY, POSSIBILITY OF PREVENTION AND ROLE OF CYTOLOGY IN SCREENING OF CERVICAL LESIONS

Submission Date: January 05, 2022, **Accepted Date:** January 15, 2022,
Published Date: January 25, 2022
Crossref doi: https://doi.org/10.37547/medical-fmspj-02-01-01

Dilfuzahon Zakirzhanovna Mamarasulova

Doctor of Medical Sciences, Associate Professor of the Department of Oncology and Medical Radiology, Andijan State Medical Institute, Uzbekistan

Doniyorbek Shuxratbekovich Khasanov

Ph.D, Docent, Department Of Oncology and Medical Radiology, Andijan State Medical Institute, Uzbekistan

ABSTRACT

This article discusses the prevention of cervical cancer and th0000000 e diagnosis of the initial stages of carcinogenesis are still the most important medical and social problems. Scientific work carried out in Uzbekistan on the analysis of the results of preventive work and the association of HPV and the use of the SCC marker in precancerous and background diseases of the cervix has not been sufficiently studied to date.

KEYWORDS

Cervical cancer, screening, cytology.

INTRODUCTION

Cervical cancer (CC) is a pathology for which the possibility of effective prevention has been proven. Preventive local treatment of preinvasive cervical lesions (so-called high-grade cervical

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 02 ISSUE 01 Pages: 1-8
SJIF IMPACT FACTOR (2021: 5.14)
OCLC – 1272874727 METADATA IF – 6.986
Publisher: Frontline Journals

intraepithelial neoplasia, HG CIN) is a generally accepted strategy with proven clinical relevance [5,6]. The progression from human papillomavirus infection (HPVI) to cervical cancer can take 15–20 years [13]. Such a long precancerous phase provides opportunities for early diagnosis and timely therapy, and also makes it possible to express the imperative about the advisability of population screening. Despite the introduction of population-based screening, invasive cervical cancer remains one of the most common malignant diseases - the fourth most frequent among malignant neoplasms in women, according to world statistics [14, 10]. In 2018, cervical cancer was diagnosed in 570 thousand women and caused death in 311 thousand. Moreover, 84% of cases and 88% of deaths from cervical cancer occur in developing countries [5].

In countries with a high organization of the health care system, there is a significant decrease in the incidence and mortality from cervical cancer, as a result of the treatment of precancerous lesions identified during the screening process [7, 11]. Also, screening measures allow identifying cases of cancer, which, with timely interventions, can reduce cancer mortality. In the UK, the incidence of cervical cancer has decreased by 24% since the introduction of the national screening program in 1988 [9]. Mortality decreased from 8/100 thousand in 1988 to 3/100 thousand women in 2017 [12, 16]. In Finland, after the introduction of population-based screening in 1960, morbidity and mortality decreased by 80%. Today, the incidence rate is 4/100 thousand and the mortality rate is 1/100 thousand women per year [8]. Trends in the dynamics of morbidity and mortality in different countries depend on various factors, including the prevalence of HPV infection and the environmental situation, the quality, and the volume of screening programs.

In the mechanism of oncogenesis, both environmental factors and changes in hormonal status, toxic effects, viral infections are important [13,6,7]. These factors disrupt epigenetic regulation of the cell cycle by methylation of promoter genes and inhibition of tumor suppressor genes [13, 4, 12].

Over the past decade, there has been significant progress in preventing the development of cervical cancer due to the inclusion of testing for the presence of HPV DNA in screening programs, as well as in connection with the introduction of preventive HPV vaccination.

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 02 ISSUE 01 Pages: 1-8
SJIF IMPACT FACTOR (2021: 5.14)
OCLC – 1272874727 METADATA IF – 6.986
Publisher: Frontline Journals

Clinical and morphological classification of pathological processes of the cervix, proposed by Ya.V. Bohman in 1989 includes 5 types of lesions [2]:

1) Background processes: ectopia, true erosion, ectropion, polyp, endometriosis, leukoplakia, erythroplakia, papilloma, and flat warts
2) Precancerous process - cervical intraepithelial neoplasia (CIN):
   - CIN1 - weak
   - CIN2 - moderate
   - CIN3 - heavy
3) Pre-invasive cancer (Ca in situ, intraepithelial cancer)
4) Micro-invasive cancer
5) Invasive cancer: squamous cell orifice, squamous cell non-keratinizing, adenocarcinoma, dimorphic glandular squamous (mucoepidermoid), poorly differentiated.

The importance of clinical and morphological classification is determined by its key role in the choice of patient management tactics: the use of local treatment methods (cytotoxic drugs, chemical and physical destruction) is possible only with pre-invasive types of lesions. Invasive cancer requires surgical removal, as well as the use of chemotherapy and radiation therapy [6, 3, 1]. WHO also proposes to classify CM epithelial dysplasias by degrees as low, moderate, and severe [9,3,7]: CIN1, CIN2, CIN3, respectively.

Exfoliative cytology has been the mainstay of pathology screening for a long time. Traditionally, cells were obtained by taking a smear with a special brush or spatula, the material was placed on glass (slide) and stained according to the method proposed by Papanicolau in the 40s of the 20th century (Pap smear). Recently, the method of liquid cytology has been used, in which the material is collected with a plastic brush immersed in a special fixation solution. The equipment for obtaining cytological material is approved for use by the responsible authorities in various countries, including the reputable American Food and Drug Administration (FDA). Liquid cytology has many advantages over the Pap smear:

- Diagnostic slides are obtained in a semi-automatic mode,
- Cell detritus, erythrocytes, leukocytes, and artifacts are removed during the smear process,

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 02 ISSUE 01 Pages: 1-8
SJIF IMPACT FACTOR (2021: 5.14)
OCLC – 1272874727 METADATA IF – 6.986
Publisher: Frontline Journals

- A thin layer of epithelial cells is formed, available for high-quality visual analysis by a morphologist,
- In the obtained material, in addition to cytological research, it can be used for HPV PCR testing, as well as the determination of other molecular markers.

Liquid cytology can reduce the proportion of poor quality slides from 9.1% to 1.6% [14].

A meta-analysis conducted during the preparation of the European Guidelines for Quality Assurance in Cervical Cancer Screening showed that although liquid cytology and traditional Pap smear show comparable characteristics of diagnostic sensitivity and specificity in terms of detecting stage 2 CIN and higher (CIN2 +), and also that liquid cytology has less specificity in terms of detecting atypical cells of undetermined value (ASC-US), liquid cytology improves the quality and speed of interpretation, as well as other molecular tests [15].

The Bethesda terminology, proposed in 1988 to describe the cytological characteristics, modified later in 2001 and 2014, makes it possible to distinguish the following types of slides [9,11]:

- Atypical epithelial cells of unclear meaning (ASC-US: HPCI) - 3-5% of all slides,
- Low-grade intraepithelial lesions (LSIL: CIN1) - 1-2% of all slides,
- High grade intraepithelial lesions (HSIL: CIN2-3) - 0.5-1% of all slides.

Pathology of glandular cells is found in 0.2% of all diagnostic slides [17].

The relationship between various cytological classifications [2] can be represented as follows (Table 1)

Table 1

Various histological classifications of cervical epithelial pathology

Pap test	class WHO system	CIN system	Bethesda system
Class 1 (norm)	Absence of malignant cells	No neoplastic changes	norm
Class 2 (metaplasia, inflammation)	Inflammatory atypia		ASCUS, ASC-H
Class 3 (dyskaryosis)	Mild dysplasia	CIN-1 (undifferentiated cells n / 3 layer)	LSIL

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 02 ISSUE 01 Pages: 1-8
SJIF IMPACT FACTOR (2021: 5.14)
OCLC – 1272874727 METADATA IF – 6.986
Publisher: Frontline Journals

	Moderate dysplasia	CIN-2 (undifferentiated cells 2n / 3 layer)	HSIL
	Severe dysplasia	CIN-3 (immature cells more than 2n / 3 layers or the entire thickness, but without invasion of the underlying layers)	
Class 4 (carcinoma in situ)	Carcinoma in situ		
Class 5 (CC)	Invasive carcinoma	Carcinoma	Carcinoma

The limitation of cytological examination is a large number of false-negative results (20% -25%). This phenomenon is associated with both the drawbacks of obtaining diagnostic slides and errors in their interpretation [18,9].

A retrospective analysis shows that in most cases (60%), the primary diagnosis of cervical cancer is recorded in women who do not have clinical manifestations of the disease, i.e. in the process of screening, in 10% of cases the disease is diagnosed at the stage of clinical manifestations due to insufficient screening programs. However, 30% of new cases of cervical cancer are not detected during screening (false-negative results of cytological examination). In addition, the cytological examination is not very effective in detecting intraepithelial lesions of the glandular epithelium located in the endocervical glands [10]. This is due to the difficulty of reaching the surface parts of the glands during sampling; as a result, these cells do not enter the test material. The incidence of glandular pathology and adenocarcinomas is progressively increasing and amounts to 20-30% of all cases of cervical cancer. This type of cervical cancer shows a significantly worse prognosis, in particular, due to late diagnosis and detection at a higher clinical stage.

REFERENCES

1. Карахалис Л.Ю., Зуева Т.П., Петренко С.И. Оптимизация терапии дисплазий шейки матки, ассоциированных с впч-инфекцией // Проблемы репродукции. – 2012. – Т.5. – С. 1–4.
2. Клиничиские рекомендации «Цервикальная интраэпителиальная неоплазия, эрозия и эктропион шейки матки». Российское общество акушеров-гинекологов (РОАГ) • Общероссийская общественная организация «Российское

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 02 ISSUE 01 Pages: 1-8
SJIF IMPACT FACTOR (2021: 5.14)
OCLC – 1272874727 METADATA IF – 6.986
Publisher: Frontline Journals

общество специалистов по профилактике и лечению опухолей репродуктивной системы» (РОСОРС) Год утверждения 2020

3. Abdumutalibova S.K., Mamarasulova D. Z., Ishanchaeva N. Q., Nabijonova G. Kh. Etiology and diagnosis of benign breast diseases and their relationship with diseases of the reproductive system in fertilized women. ACADEMICIA: An International Multidisciplinary Research Journal; ISSN: 2249-7137. (2021) Vol. 11(9): 947-952.
4. Arbyn M, Anttila A, Jordan J, Ronco G, Schenck U, Segnan N, et al. European Guidelines for Quality Assurance in Cervical Cancer Screening. Second edition--summary document. Annals of oncology: official journal of the European Society for Medical Oncology/ESMO. 2010;21:448–58. [PMC free article] [PubMed] [Google Scholar]
5. Arbyn M, Bergeron C, Klinkhamer P, Martin-Hirsch P, Siebers AG, Bulten J. Liquid compared with conventional cervical cytology: a systematic review and meta-analysis. Obstet. Gynecol. 2008;111:167–177. [PubMed] [Google Scholar]
6. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer. 2010;127(12):2893–2917. [PubMed] [Google Scholar]
7. Gustafson KS, Furth EE, Heitjan DF, Fansler ZB, Clark DP. DNA methylation profiling of cervical squamous intraepithelial lesions using liquid-based cytology specimens: an approach that utilizes receiver-operating characteristic analysis. Cancer. 2004;102(4):259–268. [PubMed] [Google Scholar]
8. Insinga RP, Glass AG, Rush BB. Diagnoses and outcomes in cervical cancer screening: a population-based study. Am. J. Obstet. Gynecol. 2004;191:105–113. [PubMed] [Google Scholar]
9. Mamarasulova D., Abduhakimov A., Tursunov D., Urmanbaeva D., Jalolov O., Isaev Z. Comparative Analysis of the Mortality Structure among the Population of Andijan Region for 2016-2018. J. Cardiovasc Disease Res., 2020; 11(2): 01 – 03.
10. Matsuo K, Machida H, Mandelbaum RS, Konishi I, Mikami M. Validation of the 2018 FIGO cervical cancer staging system. Gynecol

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 02 ISSUE 01 Pages: 1-8
SJIF IMPACT FACTOR (2021: 5.14)
OCLC – 1272874727 METADATA IF – 6.986
Publisher: Frontline Journals

Oncol. 2019;152:87–93. doi: 10.1016/j.ygyno.2018.10.026. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

11. Moore HM, Kelly AB, Jewell SD, McShane LM, Clark DP, Greenspan R, Hayes DF, Hainaut P, Kim P, Mansfield EA, Potapova O, Riegman P, Rubinstein Y, et al. Biospecimen reporting for improved study quality (BRISQ) Cancer Cytopathol. 2011;119(2):92–101. [PubMed] [Google Scholar]
12. Ronco G, Dillner J, Elfstrom KM, Tunesi S, Snijders PJ, Arbyn M, et al. Efficacy of HPV-based screening for prevention of invasive cervical cancer: follow-up of four European randomised controlled trials. Lancet. 2014;383:524–532. [PubMed] [Google Scholar]
13. Solomon D, Davey D, Kurman R, Moriarty A, O'Connor D, Prey M, Raab S, Sherman M, Wilbur D, Wright T, Jr, Young N. The 2001 Bethesda System: terminology for reporting results of cervical cytology. Jama. 2002;287(16):2114–2119. [PubMed] [Google Scholar]
14. Spathis A, Aga E, Alepaki M, Chranioti A, Meristoudis C, Panayiotides I, Kassanos D, Karakitsos P. Promoter methylation of p16(INK4A), hMLH1, and MGMT in liquid-based cervical cytology samples compared with clinicopathological findings and HPV presence. Infect Dis Obstet Gynecol. 2011;2011:927861. [PMC free article] [PubMed] [Google Scholar]
15. Torres KL, Marino JM, Pires Rocha DA, de Mello MB, de Melo Farah HH, Reis R, D. S, et al. Self-sampling coupled to the detection of HPV 16 and 18 E6 protein: A promising option for detection of cervical malignancies in remote areas. PLoS ONE. 2018;13:e0201262. [PMC free article] [PubMed] [Google Scholar]
16. Tsuda H, Hashiguchi Y, Nishimura S, Kawamura N, Inoue T, Yamamoto K. Relationship between HPV typing and abnormality of G1 cell cycle regulators in cervical neoplasm. Gynecol Oncol. 2003;91(3):476–485. [PubMed] [Google Scholar]
17. Watson M, Saraiya M, Benard V, Coughlin SS, Flowers L, et al. Burden of cervical cancer in the United States, 1998-2003. Cancer. 2008;113:2855–2864. doi:

10.1002/cncr.23756. [PubMed] [CrossRef] [Google Scholar]

18. Yakubbekova S.S., Israilov R. I., Mamarasulova D. Z., Azizov Y. D., Inaqova Z. T. (2021). Clinical And Morphological Features And Histological Variants Of Borderline Types Of Ovarian Tumors. The American Journal of Medical Sciences and Pharmaceutical Research, 3(01), 152-158.