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CASE REPORT

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Novel use of fine needle aspiration (FNA) biopsy to diagnose cervical cancer in a low-resource setting: A case series Morovia, Liberia

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Abstract

The role of pathology in improving cancer in resource-limited countries is essential, yet many barriers exist. FNA is a rapid, low-cost and efficient method for diagnosing cancer, planning treatment, and building a cancer registry.

KEYWORDS

adenocarcinoma, cervical cancer, cytology, fine needle aspiration (FNA), low- and middle-income countries (LMICs), squamous cell cancer

1 | INTRODUCTION

Fine needle aspiration (FNA) is a rapid, low-cost and minimally invasive method currently used for diagnosing a wide variety of infectious and malignant lesions in both high- and low-resource settings. Its use in cervical cancer has been important in staging and treatment planning where the role of FNA is limited to diagnosing metastasis to distant sites. Because it requires limited infrastructure, FNA is often the only first-line diagnostic tool for diagnosing cancers in many low- and middle-income countries (LMICs). In resource-poor Liberia where cervical cancer incidence is high, pathologic diagnosis of cancer is limited and treatment is often initiated based on clinical examination only. In this setting, we utilized FNA in a novel way to obtain samples directly from the cervical lesion to establish the diagnosis of cancer and histologic type prior to treatment. We diagnosed cervical cancer in 13 patients referred to the JFK Maternity Center with large visible cervical lesions. Patients ranged in age from 33 to 75 years with a mean age of 51 years. Squamous cell cancer was the predominant histologic type assessed in 12 patients and adenocarcinoma in one patient. There were no complications related to the procedure, and all patients were referred for treatment with a documented diagnosis. This information was important in not only in having a pretreatment diagnosis but it also provided the first postwar data for the development of a national cancer registry to establish the burden of disease from cervical cancer in Liberia.

In developing countries, cervical cancer remains one of the major causes of morbidity and mortality in women

worldwide. Over 80% of the >560 000 new cases of cervical cancer diagnosed globally occur in low- and middle-income countries (LMICs) where screening, diagnostic, and treatment facilities are inadequate.[1,2] Histological confirmation of cancer presenting as visible cervical lesions is often not performed in LMICs due to a range of barriers. Among the most common are the absence of pathology services, inability to pay for services if they exist, refusal of biopsy by patient, not showing up for appointments, or fear of spread of cancer following a procedure.[3] It is not uncommon therefore in developing countries that treatment is initiated based on the visible characteristics of the cervical lesion and on the bimanual examination which can be used to verify staging of suspected cervical cancers.

Pathology plays a key role in the effective provision of cancer care, yet it is often neglected in the healthcare infrastructural development in LMICs.[4] Lack of appropriate diagnosis results in the delivery of inadequate or inappropriate treatment and can compromise a country's ability to appropriately identify the burden of cancer it carries, thus making it difficult to allot budgets for national care. The barriers to quality pathology services are multiple and cannot be easily overcome without investments from both public and private sectors. In LMICs, where developing pathology services are both costly and often never ending, the introduction of fine needle aspiration (FNA) biopsies has been recognized as a cost effective and reliable method for confirming a diagnosis of palpable or visible lesions.[5]

FNA is a reliable, rapid, and noninvasive method that utilizes a small-gauged needle to aspirate cells from a mass that are then analyzed for diagnosis. While it was initially used to assess superficial palpable masses, its range has extended to include biopsy of nonpalpable masses detected by imaging methods including ultrasound, MRI, and CT scans.[6] The earliest use of what is today called fine needle aspiration dates back to the 10th century Arab literature when a physician Albucasis described therapeutic aspirations in patients with thyroid masses using needle-like instruments. During the 19th-20th century, this technique evolved into a diagnostic procedure using large bore needles to obtain tissue for diagnosis. It was not until 1931 that a German physician Mannheim reported on his use of fine needles for aspirating tumors in an attempt to avoid tumor seeding and minimize trauma from the procedure.[7] FNA today is used to diagnose a wide variety of tumors including head and neck, thoracic, intra-abdominal, breast, genitourinary, retroperitoneal, and bone.

In 2018, a fine needle aspiration (FNA) laboratory was set up at JFK Hospital in Liberia[8], It marked the first time since the end of the war that pathology services were offered in the city of Monrovia home to 1.8 Million Liberian citizens. The only other FNA services offered in the country were at the Jackson Doe Memorial Hospital in Nimba County, some 6 hours away, and barely accessible from the city during the rainy season.

This is a retrospective review of consecutive cases of cervical cancer diagnosed by FNA at JFK Hospital and submitted for data collection to the Liberian National Cancer Registry (LINCAR).

2 | METHODS

The Internal Review Board (IRB) at JFK Memorial Hospital, Liberia and at Mount Sinai Medical Center waived the need for ethics approval of the retrospectively obtained and de-identified data for this review.

We reviewed 446 FNAs performed for all causes between January 2018 and November 2018 at JFK Hospital FNA laboratory. Aspirates were taken from various sites including breast, lymph nodes, head and neck and skin, as well as 13 cases of FNAs taken from cervical lesions during the referenced period. Patients were referred from in-hospital, and from local private and public facilities. The procedure was explained to all patients who were then required to sign consent for FNA procedure; a trained cyto-pathologist (DA) performed all procedures in an outpatient setting located in close proximity to the laboratory.

2.1 | Equipment

To ensure successful procedure and diagnostics, all equipment was prepared prior to aspiration. This included 4-6 frosted glass slides, 10 and 20 cc syringes, 22 gauge needles of varying lengths, iodine solution, and jumbo tip cotton swabs and Diff-Quik stains. All materials were purchased or donated at a estimated cost of under $500 (US).

2.2 | Patient positioning and preparation

The procedure was performed with the patient in dorsal lithotomy position with the cervical lesion visible through an appropriate-sized speculum. No local anesthesia was used. After gentle cleansing of the cervical sites with iodine solution, a 10 cc syringe with an attached 22-gauge Luer Lock needle was introduced into a selected site of the visible lesion. Needle length varied and was determined by the distance to the cervical lesion. Since all lesions were clearly visible through the speculum, use of ultrasound or colposcopy to guide FNA was not required. Also, punch biopsy was

not performed out of concern for bleeding given that all lesions were large and vascular.

2.3 | Aspiration

Aspiration biopsies were obtained using a two-handed suction technique with the needle attached to an air-filled prevacuum syringe and inserted into the center of the lesion (either exophytic or ulcerative) depending on the clinical presentation of the cancer. With the needle in place, suction was applied and the needle tip was moved back and forth rapidly to achieve adequate sampling. The procedure was terminated when the presence of blood or aspirate was noted in the hub of the needle. Prior to withdrawal of the needle, suction was released to trap diagnostic material in the bore of the needle. Needles were flushed under pressure onto frosted slides that were smeared. Between two and three aspirations were obtained from the center of the tumor and from the cervix at the interface between normal mucosa and lesion, from each patient based on specimen adequacy. Specimen adequacy determined the number of aspirations obtained; a range of 2-4 passes was made with an average of 2 passes per patient. Upon final withdrawal of the needle, manual pressure was applied to the aspirate sites to ensure no biopsy-related bleeding. The average time from patient entry to completion of the procedure was 15 minutes. The patients were observed for possible complications from the procedure before discharge.

2.4 | Handling of aspirates

Once withdrawn from the cervix, the needle was detached from the syringe and air was drawn into the syringe. The needle was replaced, and the aspirate was expelled onto several glass slides. Slides were lightly smeared to avoid crushing and nuclear damage. Smeared slides were transported to the adjacent laboratory for processing and rapid interpretation. All slides were stained using a differential quick method (Diff-Quik) which was donated by our collaborators; additional slides were also stained with rapid Papanicolaou staining if kits were available. Diff-Quik is a rapid commercial stain that consists of three solutions: a fixative, an eosinophilic stain, and a basophilic stain. The rapid Pap stain uses a standard nuclear stain and two cytoplasmic counter stains. The slides were air-dried and the standard staining protocol was followed for Diff-Quik staining. Slides were immediately scanned for adequacy and diagnosis. At the completion of the staining process, slides were rinsed with distilled water and placed in a vertical position to dry, avoiding wiping, or blotting with tissue paper to preserve cell integrity. Once slides were entirely dried, detailed microscopic examination was performed and reports issued.

3 | RESULTS

Thirteen symptomatic patients with visible cervical lesions suspicious for cervical cancer underwent FNA biopsy. (Table 1) Average age of patients was 51 years with a range of 33-75 years. Lesion size ranged from 3 to 8 cm; both exophytic and ulcerative lesions were present. Patients were referred from inpatient (n = 6), outpatient (n = 4), outside hospitals (n = 2), and self-referral (n = 1). Twelve patients were diagnosed with squamous cell carcinoma, and only one had a diagnosis of adenocarcinoma of the cervix.

In all cases, FNA provided sufficient cells for diagnosis. The majority of aspirates were diagnostic for squamous cell carcinoma of the cervix (Figure 1- Diff-Quik). The features seen were of both keratinizing and nonkeratinizing subtypes. The microscopic feature of the keratinizing variant showed sheets of highly atypical crowded hyperchromatic spindle-shaped cells with prominent nuclei, coarse chromatin patterns, and cytoplasmic ringing in a background of tumor diathesis (Figure 2 Diff-Quik). The nonkeratinizing variant showed sheets of hyperchromatic cells with scant cytoplasm (Figure 3 Diff-Quik). The nuclei displayed prominent nucleoli and highly irregular chromatin distribution with areas of clearing between clumps. The cells had a background of degenerative cellular debris and blood. The one case of adenocarcinoma of the cervix showed a three-dimensional cluster of hyperchromatic cells with abundant cytoplasm and marked nuclear atypia. There were no procedure-related complications.

TABLE 1 Patient Referral Information

	Mean	Range
Age	51	33-75
	N	%
Diagnosis		
Squamous cell carcinoma of the cervix	12	92.3
Adenocarcinoma of the cervix	1	7.7
Inpatient	6	46.1
Outpatient	4	30.8
Outside Hospital	2	15.4
Self-referral	1	7.7
Symptoms		
Vaginal bleeding	9	46.1
Foul vaginal odor	2	30.8
Pain	1	15.4
Combination of symptoms	8	7.7

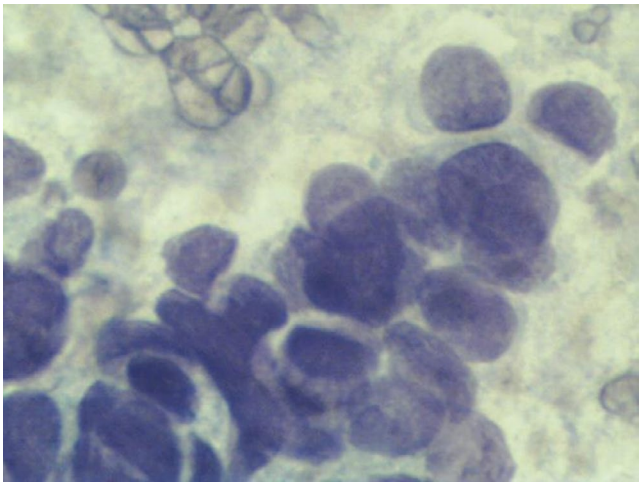

FIGURE 1 Carcinoma cells with hyperchromatic nuclei, marked variation of nuclear size, coarse chromatin with clearing, and minimal cytoplasm

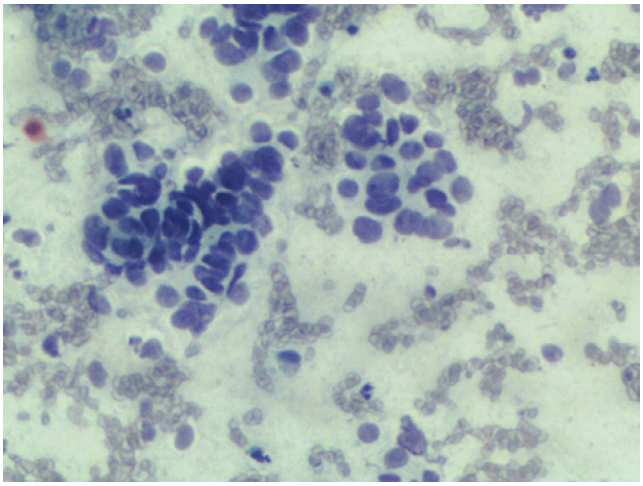

FIGURE 3 Clusters of carcinoma cells with hyperchromatic nuclei, scant cytoplasm, high nuclear: cytoplasmic ratio, and marked nuclear size variation with coarse chromatin

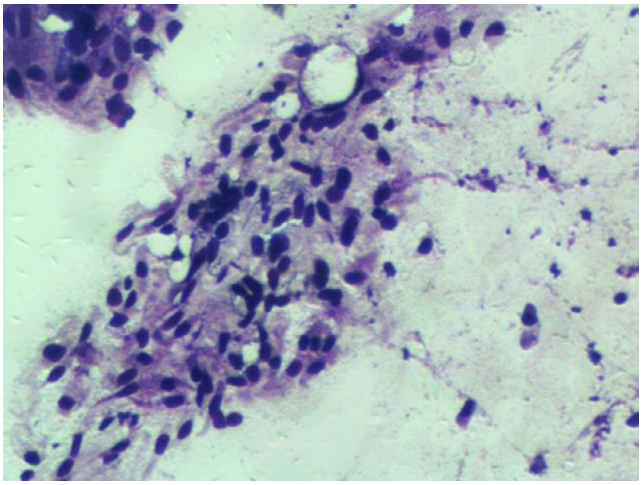

FIGURE 2 Cluster of pleomorphic, spindled, keratinizing carcinoma cells with hyperchromatic nuclei, marked variation of nuclear size, and tumor diathesis in the background

4 | DISCUSSION

Fine needle aspiration biopsy findings from 13 symptomatic patients with visible cervical lesions are reported from Liberia, one of the lowest resourced countries in the world. All samples were considered satisfactory for cytological diagnosis, and in all 13 cases, cervical cancer was successfully diagnosed. The use of cytology for detecting cervical cancers predates Dr George Papanicolaou's presentation in 1928, which describes the detection of cancer cells from a patient's vaginal secretions. Sir John Williams (1886) proposed the presence of benign lesions that preceded the onset of cervical cancer based on biopsy samples; a concept that was later supported by a handful of pathologists between 1908 and 1912.[9] The Romanian physicians Drs. Aurel Babes and Constantin Daniel, however, emphasized the theory of a precancerous lesion when they presented data in 1927 using a platinum loop to collect cervical cytology smears that were fixed with methanol and stained with Giemsa for diagnosing cancer.[10] Over time, Babe's methodology for cervical cancer detection was largely replaced by Papanicolaou's exfoliative cytology. Although this method was not well received initially, Papanicolaou's continued collaborative efforts in refining the methodology resulted in his landmark presentation in 1941 defining what we today know as the Papanicolaou smear.

Aspiration cytology in the United States was widely performed at Memorial Hospital in New York in the 1930s, but the technique really took hold in Sweden at the Karolinsa Hospital in the 1950's and 1960's garnering international attention. The resurgence of FNA in the 1970s in the United States has resulted in it being one of the most frequently used evaluations for diagnosing cancer today.[11] There is some variation in reported sensitivity of FNA biopsy; however, sensitivity appears to be most strongly influenced by sample adequacy and timely evaluation of specimens. Gomez-Macias et al demonstrated that for most lesions, adequate samples were most often obtained when a pathologist performed the FNA or supervised a pathology resident doing the procedure, emphasizing the importance of operator experience for obtaining quality specimens.[12] Immediate reading of FNAs is recommended as it serves a dual purpose. It allows the pathologist to assess the adequacy of the sample and serves to decrease false negative rates, increasing the sensitivity of the procedure.[13] In our study, the same pathologist performed all FNA biopsies, and staining and interpretation were done immediately. When available, both Diff-Quik stained and rapid Papanicolaou stained slides were used for interpretation as Papanicolaou stains appeared to provide better enhancement

of nuclear detail and nucleolar features in keratinized squamous cells. The ultrafast Papanicolaou (UFP) with a turnaround time of 90 seconds and Toluidine blue, a rapid and low cost effective stain, also provide good nuclear detail on FNA aspirates; however, neither of these stains was unavailable in Liberia for use in our clinic.

The most commonly diagnosed cervical malignancy in our study was squamous cell carcinoma. This finding correlates with findings elsewhere in which squamous cell carcinoma is the most common cancer of the cervix. Gaya et al also encountered maximum cases of squamous cell carcinoma in their studies.[14] This finding is explainable as squamous cell carcinoma accounts for the vast majority of cervical malignancies in sub Saharan Africa with the etiological agent being oncogenic HPV serotypes.[15] In the present study, one case was diagnosed as adenocarcinoma. All the patients in this study had late presentation, (bulky stage IIB –IV) which is similar to the presentation seen in most low-resource settings and in a previous assessment of cervical cancer in Liberia.[16,17] The low number of cases diagnosed in this case series does not reflect the prevalence of disease, but can be attributed to limited referral for biopsy since most referring centers were not aware of the availability of FNA biopsy taken directly from the cervix.

The application of FNA to the diagnosis of oral mucosal head and neck lesions is preferred over open biopsy in selected cases due to its lower risk of complications including risk of seeding, bleeding, and discomfort while allowing the clinician to prioritize imaging and further work up.[18] Despite these advantages, this procedure has not been previously reported for cervical cancer. Since most women present with late stage cervical lesions, and control of complications during or in the immediate period after punch biopsy presents a challenge, the use of a thin bore needle which permits little manipulation of the lesions and limits bleeding provides some advantages.

This is the first published report on the use of FNA for diagnosing cancer from visible cervical lesions seen on speculum examination. Other reports of cervical cancer diagnosis using FNA have been limited to evaluation of metastatic sites such as the mediastinum,[19] supraclavicular nodes,[20] retroperitoneal nodes,[21] or intra-abdominal masses.[22] Cendrowski et al[23] additionally demonstrated the upstaging of clinically staged cervical cancer IB by preoperative assessment of parametria using FNA and trans-vaginal sonography (TVS) with 71% sensitivity and 86% specificity. With the recently updated FIGO clinical staging for cervical cancer,[24] incorporating metastatic assessment by either imaging or FNA biopsy, these metastatic evaluations with FNA will now be of increasing importance.

One of the limitations of this report is the inability to compare FNA aspirates for accuracy, using histology as the gold standard. Similarly, lack of infrastructure to provide immunohistochemistry as a complimentary tool in the identification of poorly differentiated or mixed tumors is a drawback to the diagnostic capacity of the laboratory.

5 | CONCLUSION

While the described technique is most suitable for low-resource countries where histopathology is not available, it has applicability in any situation where patients present with large cervical lesions that are aggressively bleeding and where a rapid diagnosis is needed in order to initiate emergency treatment. In Liberia, FNA is currently the only method of diagnosing cancer; the use of FNA for cancer diagnosis simultaneously allows Liberia to enhance its cancer registration capacity and quantitate its burden of cancer. With full histopathology services scheduled to begin in 2019 at JFK Hospital, a larger study will be initiated comparing the cytological diagnosis using FNA to the gold standard to determine the accuracy, specificity, and sensitivity of this procedure.

CONFLICT OF INTEREST

I declare there is no conflict of interest.

AUTHOR CONTRIBUTIONS

DA and AMB: conceived the presented idea and co-wrote the first draft of the manuscript. DA: devised the technique and performed all FNAs. AMB: took the lead in reconfiguring the manuscript for Clinical Case Reports with input from all authors. BD and SC: implemented FNA laboratory, provided critical feedback and editing of manuscript. ML and AD: researched references, edited manuscript and selected and uploaded photographs with input from Dr Alele. EPG, EI, and BJ: provided critical feedback and edited manuscript.

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REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2018;68(6):394-424.
2. LaVigne AW, Triedman SA, Randall TC, Trimble EL, Viswanathan AN. Cervical cancer in low and middle income countries: addressing barriers to radiotherapy delivery. *Gynecol Oncol Rep*. 2017;22:16-20.
3. Mwaka AD, Orach CG, Were EM, Lyratzopoulos G, Wabinga H, Roland M. Awareness of cervical cancer risk factors and symptoms: cross-sectional community survey in post-conflict northern Uganda. *Health Expect*. 2016;19(4):854-867.

4. Sayed S, Lukande R, Fleming KA. Providing pathology support in low-income countries. *J Glob Oncol*. 2015;1(1):3.
5. Benediktsson H, Whitelaw J, Roy I. Pathology services in developing countries: a challenge. *Arch Pathol Lab Med*. 2007;131(11):1636-1639.
6. Kocjan G, Chandra A, Cross P, et al, BSCC code of practice–fine needle aspiration cytology. *Cytopathology*. 2009;20(5):283-296.
7. Diamantis A, Magiorkinis E, Koutselini H. Fine-needle aspiration (FNA) biopsy: historical aspects. *Folia Histochem Cytobiol*. 2009;47(2):191-197.
8. Fischer G, Beddoe A, Alele D. Reestablishing diagnostic anatomical pathology services by a fine-needle aspiration clinic in Monrovia, Liberia. *Am J Clin Pathol*. 2018;150(suppl_1):S90-S90.
9. Shaw PA. The history of cervical screening I: the Pap. Test. *J SOGC*. 2000;22(2):110-114.
10. Krafts K, Pambuccian S. Romanowsky staining in cytopathology: history, advantages and limitations. *Biotech Histochem*. 2011;86(2):82-93.
11. Pradhan P. History of fine needle aspiration cytology: trials and triumphs - a brief review. Vol 20 2017.
12. Gomez-Macias G, Garza-Guajardo R, Segura-Luna J, Barboza-Quintana O. Inadequate fine needle aspiration biopsy samples: Pathologists versus other specialists. *CytoJournal*. 2009;6:9.
13. Silverman JF, Frable WJ. The use of the Diff-Quik stain in the immediate interpretation of fine-needle aspiration biopsies. *Diagn Cytopathol*. 1990;6(5):366-369.
14. Gaya SA, Yakasai IA, Muhammad AZ, Galadanci HS, Garba ID. Cancer of the cervix in unscreened West African women. *J Basic Clin Reprod Sci*. 2012;1(1–2):44-48.
15. Mboumba RB, Prazuck T, Lethu T, Meye J, Bélec L. Cervical cancer in sub-Saharan Africa: an emerging and preventable disease associated with oncogenic human papillomavirus. *Med Sante Trop*. 2017;27(1):16-22.
16. Dunyo P, Effah K, Udofia EA. Factors associated with late presentation of cervical cancer cases at a district hospital: a retrospective study. *BMC Public Health*. 2018;18(1):1156.
17. Beddoe AM, Nair N, Jallah W, et al.Cervical cancer in liberia: identifying existing gaps in infrastructure and treatment availability. *Ann Carcinog*. 2018;3(1):1015.
18. Pynnonen MA, Gillespie MB, Roman B, et al, Clinical practice guideline: evaluation of the neck mass in adults. *Otolaryngol Head Neck Surg*. 2017;157(2_suppl):S1-S30.
19. Krishna SG, Ghouri YA, Suzuki R, Bhutani MS. Uterine cervical cancer metastases to mediastinal lymph nodes diagnosed by endoscopic ultrasound-guided fine needle aspiration. *Endosc Ultrasound*. 2013;2(4):219.
20. Rao S, Schwarz J, Grigsby P. Outcome of patients with occult supraclavicular lymph node metastasis from cervical carcinoma. *Int J Radiat Oncol Biol Phys*. 2010;78(3):S419.
21. Nagano T, Nakai Y, Taniguchi F, et al, Diagnosis of paraaortic and pelvic lymph node metastasis of gynecologic malignant tumors by ultrasound-guided percutaneous fine-needle aspiration biopsy. *Cancer*. 1991;68(12):2571-2574.
22. Oh MJ, Lee JS, Lee SH. A case of metastatic lymph node of invasive cervical cancer diagnosed by endoscopic ultrasonography-guided fine needle aspiration biopsy. *Korean J Helicobacter Up Gastrointest Res*. 2012;12(3):207-211.
23. Cendrowski K, Sawicki W, Spiewankiewiez B, Stelmachow J. The importance of fine needle aspiration biopsy and sonographic evaluation of parametria in cervical cancer. *Eur J Gynaecol Oncol*. 2003;24(5):413-416.
24. Bhatla N, Aoki D, Sharma DN, Sankaranarayanan R. Cancer of the cervix uteri. *Int J Gynecol Obstetr*. 2018;143(S2):22-36.

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