The merit of urine cytology in identifying cytological abnormalities in women experiencing abnormal discharge

Abstract:

Background: Urine cytology is a diagnostic method that aids in identifying various types of pathological abnormalities within the urinary system. The aim of this study was to evaluate the effectiveness of urine cytology in identifying cytological abnormalities in women experiencing abnormal discharge. **Methodology:** This investigation was carried out as a prospective descriptive study aimed at assessing the effectiveness of urine cytology in identifying cytological abnormalities in women who present with abnormal vaginal discharge. The investigation took place at High Care Private Clinic, located in El-Obeid, North Kordofan State, Sudan. The sample size of 90 encompassed all patients presenting with gynecological complaints linked to abnormal vaginal discharge who underwent a Pap test for diagnostic purposes during the timeframe from March 2024 to October 2024. **Results:** Positive cytological evidence of HPV was observed in 10% of patients. Most cases demonstrate a prevalence of polymorphonuclear inflammatory cells at 88.8%, followed by lymphocyte cells at 87.7%. Plasma cells were identified in 6.6% of cases. **Conclusion:** Urine cytology may not serve as an alternative to a cervical smear for identifying cytological atypia. The non-invasive procedure of urine cytology can be utilized to identify various infectious and inflammatory conditions.

Keywords: cytological, urine cytology, women, HPV, discharge

Introduction:

Currently, urine cytology has expanded its applications significantly, evolving from its initial role in identifying red blood cells or parasites to its current function in detecting cancer cells that are shed in urine samples [1]. The predominant cause of cervical cancers is the infection by high-risk HPV, which underscores the importance of standard screening methods, including urine cytology, in facilitating the early detection of cervical neoplasia [2].
The invasive nature of Pap smears for cervical cancer diagnosis, combined with the conservative cultural practices in developing countries, highlights the significant interest in discovering less invasive biomarkers. Quantitative label-free mass spectrometry was utilized to identify potential biomarkers in the urine samples of patients diagnosed with cervical cancer. This method was employed to investigate the differences in urinary proteome expression between healthy individuals and those with cancer. The changes in urinary proteome levels between normal individuals and cancer patients were examined using Progenesis label-free software. The findings indicated that 60 proteins were upregulated, whereas 73 proteins were downregulated in patients diagnosed with cervical cancer [3].
The identification of HPV evidence in urine shows potential as an alternative method for cervical

cancer screening; however, the validated assay for urine HPV requires further revision [4]. The World Health Organization (WHO) has advised the use of Visual Inspection with Acetic Acid (VIA) testing or, if possible, Human Papillomavirus (HPV) DNA testing for cervical cancer screening in low-resource settings. Nonetheless, a restricted number of women are able to participate in these screening programs due to the elevated costs and the invasive nature of the sampling process. While it may not be suitable as a screening tool for HPV DNA due to its low sensitivity, the urine sampling method is cost-effective and more socially acceptable for conducting large epidemiological surveys in developing countries to assess the burden [5]. The aim of this study was to evaluate the effectiveness of urine cytology in identifying cytological abnormalities in women experiencing abnormal discharge.

Materials and methods:

This study was carried out as a prospective descriptive investigation to assess the effectiveness of urine cytology in identifying cytological abnormalities in women who present with abnormal vaginal discharge. The research took place at High Care Private Clinic in El-Obeid, located in North Kordofan State, Sudan. The sample size of 90 comprised all patients presenting with gynecological complaints related to abnormal vaginal discharge who underwent a Pap test for diagnostic purposes during the period from March 2024 to October 2024. The patient's crucial identification information was gathered through a carefully designed questionnaire. The information concerning diagnostic insights was gathered after the collection of cervical and urine cells, which were then stained using the Papanicolaou procedure for cytology.

Sample collection:

Urine Sample: Completely voided urine was collected in a cleaned, dried container and promptly centrifuged, with the supernatant discarded. A drop of gelatin was added to the deposit, stirred, and spread on a cleaned frosted end glass slide. The slide was promptly fixed in 90% ethyl alcohol for 15 minutes before being stained using the Papanicolaou staining process [6].

Cervical samples:

Cervical cells were obtained by scraping the transformation zone (ecto-cervix) with an Aryl spatula. The collected cells were smeared onto a cleaned glass slide and promptly fixed in 90% ethyl alcohol while still wet. The smears were subsequently stained using the Pap procedure. Urine smears and cervical smears were first assessed for staining quality prior to cytological evaluation. Samples that were inadequate or exhibited non-optimal preservation or staining were subjected to resampling.
Cytological evaluation was conducted utilizing a grading system, following the methodology established by Ahmed et al. [7].

Results:

This study examined 90 patients presenting with abnormal vaginal conditions, aged between 20 and 55 years, with a mean age of 34.98 and a standard deviation of ± 8.007.
The distribution of the study subjects by parity and inflammatory cells is summarized in Table 1

and Figure 1. The majority of cases demonstrate a positive presence of polymorphonuclear inflammatory cells, with 80 out of 90 (88.8%), followed closely by lymphocyte cells at 79 out of 90 (87.7%). Plasma cells were detected in 6 out of 90 samples, representing 6.6% of the total. The infiltration of polymorphonuclear inflammatory cells was predominantly noted in multipara, followed by nullipara and para1, accounting for 38/80 (47.5%), 23/80 (28.7%), and 14/80 (17.5%), respectively.

A significant presence of lymphocyte inflammatory cell infiltration was noted primarily in multipara, followed by nullipara and para1, accounting for 36/79 (45.5%), 24/79 (30.3%), and 14/79 (17.7%), respectively.

Table 1 presents the distribution of study subjects categorized by parity and the presence of inflammatory cell infiltrates.

Variable	Nullipara n=26	PG n=1	Para1 n=16	multipara n=39	Grand n=8	Total n=90
Lymphocyte cells						
Present	24	1	14	36	4	79
Absent	2	0	2	3	4	11
Plasma Cells						
Absent	25	1	14	37	7	84
Present	1	0	2	2	1	6
Polymorphonuclear cells						
Present	23	1	14	38	4	80
Absent	3	0	2	1	4	10

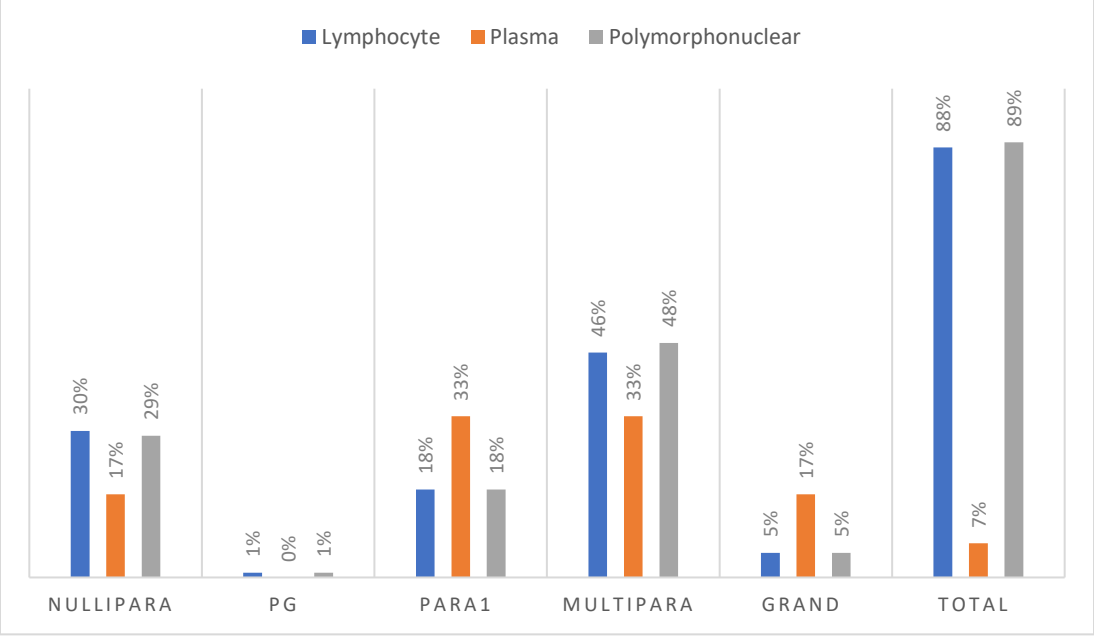

Figure 1: Description of study subjects categorized by parity and inflammatory cell presence.
Table 2 and Figure 2 illustrate the distribution of study subjects according to parity and HPV cytological evidence. Positive cytological evidence of HPV was identified in 9 out of 90 patients (10%). Most infections were associated with Para1, with multipara and grand multipara representing 3 out of 9 (33.3%) and 2 out of 9 (22.2%), respectively.
Table 2 presents the distribution of study subjects categorized by parity and infectious agent.

Variable	Nullipara n=26	PG n=1	Para1n=16	multipara n=39	Grmultipara n=8	Total n=90
Evidence of HPV						
Present	1	1	3	2	2	9
Absent	25	0	13	37	6	81
Candida Albicans						
Present	2	0	0	5	2	9
Absent	24	1	16	34	6	81

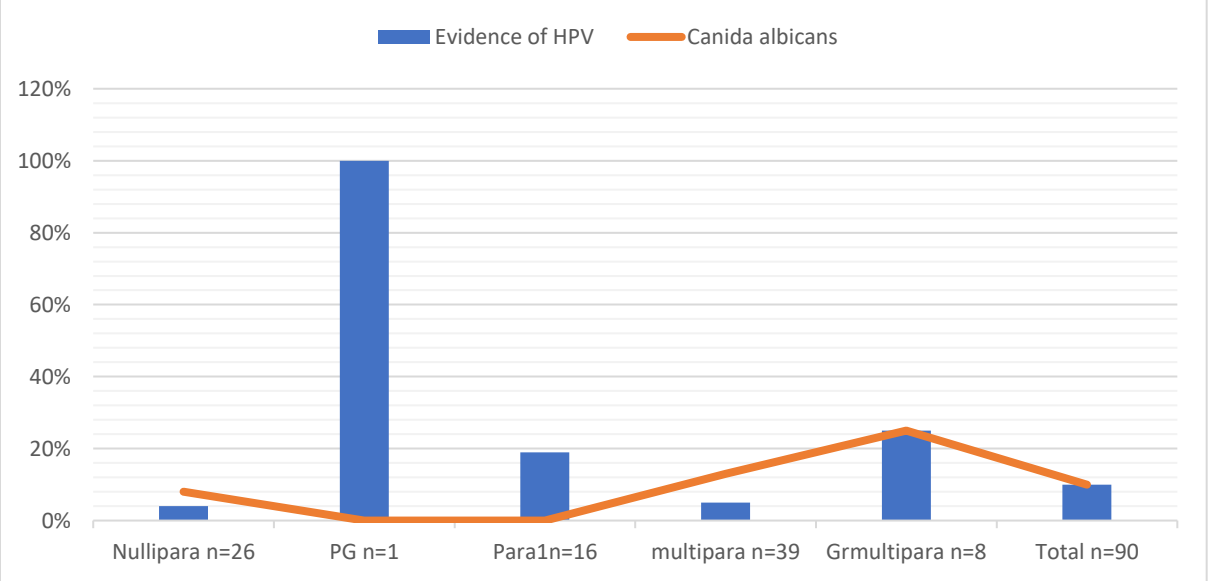

Figure 2: Description of study participants categorized by parity and presence of HPV and Candida albicans.
Table 3, Fig. 3 provide a summary of the distribution of study subjects categorized by polymorphonuclear and lymphocyte cells, as well as cytological atypia in relation to discharge color. The majority of cases demonstrate a positive presence of polymorphonuclear and lymphocyte cells, accompanied by a whitish discharge in 57 out of 80 cases (71.2%) and 56 out of 80 cases (70%). This is followed by a yellowish color observed in 14 out of 80 cases (17.5%) and 14 out of 80 cases (17.5%), respectively. In the analysis, cytological atypia was observed in 7 out of 90 cases (7.7%) with whitish discharge, while only one case (1.1%) exhibited yellowish discharge.
Table 3 provides a summary of the distribution of study subjects categorized by

polymorphonuclear and lymphocyte cells, as well as cytological atypia in relation to discharge color.

Variable	Whitish n=65	Yellowish n=15	Greenish n=5	Brownish n=5	Other n=3	Total
Polymorphonuclear						
Present	57	14	2	4	3	80
Absent	8	1	0	1	0	10
Lymphocyte cells						
Present	56	14	2	4	3	79
Absent	9	1	0	1	0	11
Cytological Atypia						
Absent	58	14	2	5	3	82
Present	7	1	0	0	0	8

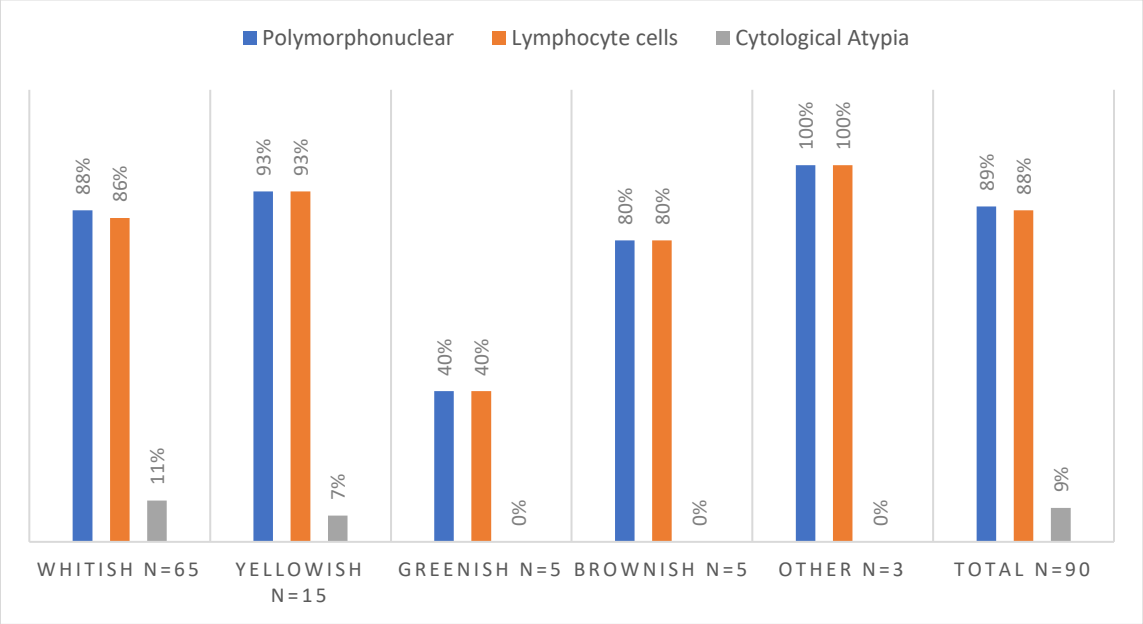

Figure 3. Description of the study participants categorized by discharge color and the presence of inflammatory cells

Table 4 and Fig 4 illustrate the distribution of study subjects based on age and cytological evidence of HPV and Candida albicans. Findings indicate that candida albicans is present in equal proportions among the age group of 36-40 years and those aged 41 years and older, with a prevalence of 3 out of 9, or 33.3%. Evidence of HPV was predominantly observed in the group aged 41 years and older, with a prevalence of 4 out of 8, or 50%. **Table 4 illustrates the distribution of study subjects according to age, as well as the cytological evidence of HPV, Candida albicans, and the presence of cytological atypia.**

Variable	≤25 years	26-30	31-35	36-40	≥41	Total

Candida albicans						
Absent	10	18	17	17	19	81
Present	1	1	1	3	3	9
Total	11	19	18	20	22	90
Evidence of HPV						
Absent	10	19	17	18	18	82
Present	1	0	1	2	4	8
Cytological Atypia						
Absent	9	17	16	18	22	82
Present	2	2	2	2	0	8

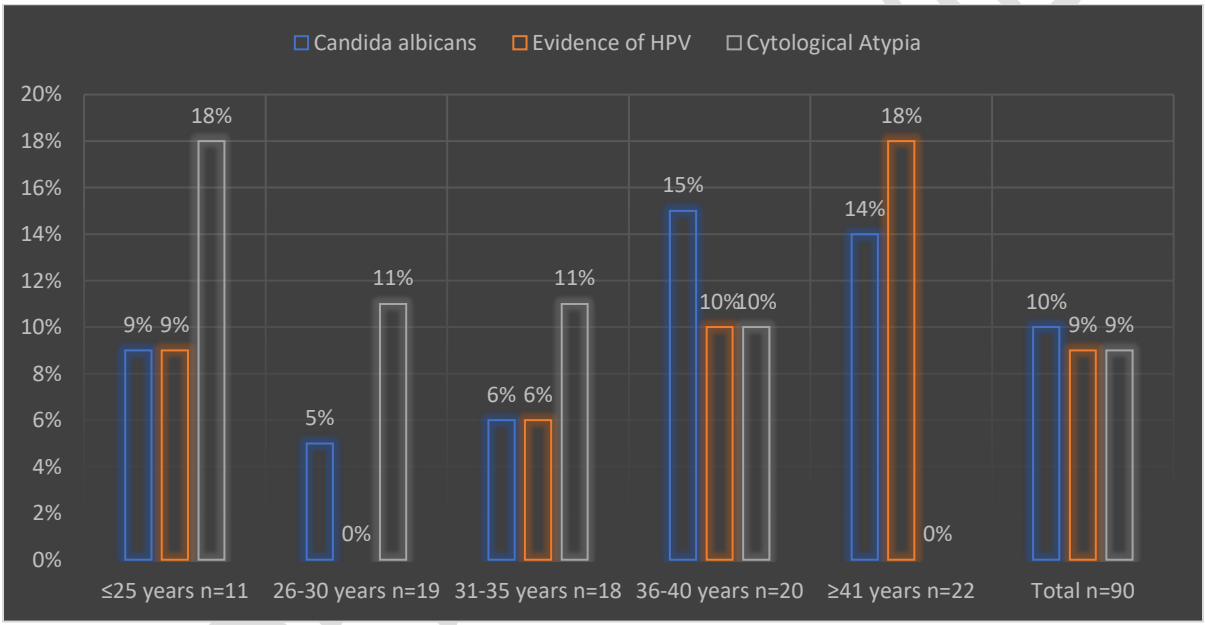

Figure 4. Description of the study subjects by age and cytological atypia, Evidence of HPV and Candida albicans

Discussion:

Despite the continuous advancements in diagnostic technology, conventional methods still present challenges for communities affected by disasters and conflicts. These situations often lead to a decline in health systems, resulting in a shortage of essential diagnostic tools. Such conditions may prompt health service providers to consider cost-effective and readily accessible alternatives. As a result, we considered the value of urine cytology in diagnosing the abnormalities linked to complaints of abnormal vaginal discharge.
This study examines two measures of abnormalities that may be linked to vaginal discharge: non-neoplastic changes and those associated with cellular proliferative activities.
In relation to cellular proliferative activity, we conduct a comparison of urine samples and cervical

smears. We identified 8 cases of cervical cytological atypia; however, none were found in urine. The term "atypia" is frequently utilized in diagnostic surgical and cytopathology, despite its lack of clear characterization. The absence of guidelines concerning the application of this term leads to its frequent use as a catch-all category. The reported rate of atypia in urine cytology varies significantly, ranging from 1.9% to 23%. This review outlines various cytomorphologic findings in urine cytology linked to established and specific causes. Urine specimens exhibiting morphologic changes linked to specific etiologic factors should be reclassified as "atypical." These consist of urine specimens displaying reactive umbrella cells or seminal vesicle cells, reactive alterations due to stones, cytologic changes indicative of infectious processes or therapeutic effects, instrumented urines with pseudopapillary clusters, and urinary diversion specimens [8].
In recent decades, the extensive adoption of HPV-related biomarkers and advancements in computerization within liquid-based cytology have led to significant improvements in the screening processes for lower genital tract malignancies across various regions globally. Numerous structured anogenital cancer prevention initiatives have arrived at a stage where effectiveness hinges more on population reach than on the existing infrastructure. Meanwhile, self-sampling methods, where individuals collect biological material (such as vaginal secretions, urine, etc.) rather than having it obtained by a clinician, are increasingly recognized for their effectiveness in testing for HPV biomarkers. Gone are the days of initial skepticism regarding the notion that vaginal or urine HPV signifies merely "passenger" transient infections; substantial scientific efforts have been undertaken to enhance the detection of high-risk HPV (hrHPV) from this "novel" biological material. Currently, numerous advanced meta-analyses have demonstrated that self-sampling methods utilizing urine self-sampling offer a viable alternative strategy, potentially improving population coverage while exhibiting outstanding performance and sensitivity. A recent review of published scientific work on urine HPV has been conducted, and following a critical appraisal, several key points should be taken into account regarding the clinical application of HRHPV urine measurements. (i) utilization of first-void urine (FVU) along with specifically designed collection devices; (ii) implementation of a preservation medium to prevent degradation of human/HPV DNA during extraction and storage; (iii) application of polymerase chain reaction (PCR)-based assays, preferably with genotyping capabilities; (iv) processing an adequate volume of whole urine; and (v) employing an analytically sensitive HPV test/recovery of cell-free HPV DNA alongside cell-associated DNA [9].
A study was conducted on the clinical and pathologic features of 17 cases of papillary serous adenocarcinoma of the cervix (PSCC) in women aged 26 to 70 years. The data revealed a bimodal age distribution, characterized by one peak prior to the age of 40 years and another peak following the age of 65. The observed symptoms included abnormal vaginal bleeding in 11 patients, abnormal exfoliative cervical cytology in four patients, and watery vaginal discharge in two patients. During the pelvic examination, eight patients presented with a polypoid or exophytic cervical mass, while two patients exhibited an ulcerated or indurated cervix. No abnormalities were observed in seven patients. Two tumors were classified as stage Ia, twelve as stage Ib, two as stage II, and one as stage III. A total of nine patients underwent radical hysterectomy, while one patient had a simple hysterectomy; additionally, six of these patients

were administered postoperative radiotherapy. The remaining patients underwent primary radiotherapy. Upon microscopic examination, the tumors exhibited a complex papillary architecture characterized by epithelial stratification and tufting. There were six tumors classified as grade 2/3 and eleven tumors classified as grade 3/3. Each of the tumors exhibited more than 10 mitotic figures per 10 high-power fields. A pronounced acute and chronic inflammatory infiltrate was characteristically observed within the cores of the papillae and in regions of stromal invasion. In three cases, occasional psammoma bodies were observed. Out of 12 tumors, five exhibited positive staining for p53, while six and nine of the 12 tumors showed immunoreactivity for carcinoembryonic antigen and CA-125, respectively. Seven tumors were combined with a different histologic subtype of cervical adenocarcinoma, predominantly low-grade villoglandular adenocarcinoma. A total of fifteen patients were monitored over a period ranging from 6 months to 11 years, with an average follow-up duration of 56 months. Six patients succumbed to extensive metastases within 5 years of their diagnosis; another patient faced tumor recurrence accompanied by malignant ascites 2 years post-diagnosis. The predominant sites of metastasis were the pelvic and periaortic lymph nodes, with additional locations including cervical lymph nodes, lung, peritoneum, liver, and skin. At the most recent follow-up, eight patients were alive and showed no signs of tumor presence. Factors such as age under 65 years, stage greater than I, tumor size exceeding 2 cm, tumor invasion beyond 10 mm, the presence of lymph node metastases, and elevated serum CA-125 levels were linked to a poor prognosis. The grade or composition of the tumor, whether pure or mixed, showed no correlation with patient outcomes. Papillary serous adenocarcinoma of the cervix exhibits microscopic similarities to its counterparts found in other regions of the female genital tract and peritoneum. The tumors may exhibit aggressive behavior, particularly with supradiaphragmatic metastases, leading to a rapidly fatal progression when identified at an advanced stage. However, the prognosis for patients with stage I tumors aligns closely with that of individuals diagnosed with the usual type of cervical adenocarcinomas [10].

Conclusion

Urine cytology may not serve as a replacement for a cervical smear in identifying cytological atypia. Urine cytology, a non-invasive procedure, can be utilized to identify various infectious and inflammatory conditions.

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