



Pelvic examination: an iatrogenic cause of microscopic hematuria in women?

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Abstract

Introduction and hypothesis Microscopic hematuria (MH) in women is a common incidental finding that can trigger morbid and costly investigation. Identifying non-pathologic etiologies of MH may help limit unnecessary investigation. Our study aimed to determine whether pelvic examination (PE) increases the prevalence of MH in women.

Methods Between May 2018 and October 2018, 157 women > 18 years of age and presenting to the Obstetrics and Gynecology private clinics at a tertiary care center were approached and asked to provide two urine samples: one before PE and one after. Samples were then analyzed to assess for the presence of MH. The McNemar test was used to evaluate whether the conversion from no MH to MH could be attributed to PE rather than to chance. An associated $p < 0.05$ was determined to be significant. Chi-square test was used to determine whether this conversion is influenced by age and menopausal status.

Results Thirteen women (8.3%) had MH before PE. Of 144 participants with no initial MH, 22 (15.3%) had MH after PE. PE was significantly correlated with the conversion from no MH to MH ($p = 0.002$). The conversion from no MH to MH following PE was not correlated with age ($p = 0.451$) or menopausal status ($p = 0.411$).

Conclusions PE performed within an hour before urinalysis was found to be a risk factor for MH in women.

Keywords Iatrogenic disease · Microscopic hematuria · Pelvic examination · Urinalysis

Abbreviations

MH	Microscopic hematuria
PE	Pelvic examination
RBCs/HPF	Red blood cells per high-powered field

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Introduction

Urinalysis is a frequently performed test in various healthcare settings for numerous diagnostic purposes. Microscopic hematuria (MH) is detected in 2.4 to 31.1% of asymptomatic individuals [1]. MH is a common reason for referral to urologists, accounting for 2.7% of the number of visits to urologists in 2012 in one study [2].

The definition of MH is not uniform among existing guidelines [3]. The American Urological Association (AUA) adopts a non-gender-specific definition of asymptomatic MH as the presence of three or more red blood cells per high-powered field (RBCs/HPF) on urinalysis of a single, “properly collected” urine sample [1]. The Canadian Consensus Statement requires two urine samples with more than three RBCs on HPF to classify as MH [4]. On the other hand, the European Association of Urology does not specify a particular threshold for RBCs to define MH [3].

MH stems from either urologic or nephrologic causes, ranging from minor findings that do not require treatment to life-

threatening conditions, of which malignancy is of particular concern. Studies have shown that the overall urinary tract malignancy rate in asymptomatic male and female individuals diagnosed with MH is approximately 2.6% [1]. This rate varies depending on the population risk factors for urinary tract malignancy, which include male gender, age, smoking, history of gross hematuria, and history of pelvic irradiation [1].

Although there is a consensus regarding the need to fully investigate patients with gross hematuria, there is inconsistency among major professional organizations and societies regarding the optimal management and extent of evaluation needed for patients with MH [3]. Common diagnostic approaches used for evaluation of MH include CT urography and cystoscopy, both of which carry financial consequences in addition to potential morbidity.

To raise the threshold for investigating MH in women, contributory factors to transient MH, such as exercise, recent menstruation, and sexual activity prior to urinalysis need to be excluded [1, 4]. Furthermore, given the low risk of malignancy in women relative to their male counterparts, specific approaches to evaluation of MH in women were suggested in a joint committee opinion by The American College of Obstetricians and Gynecologists (ACOG) and the American Urogynecologic Society (AUGS) published in 2017 [5].

Given how commonly a pelvic examination (PE) is performed, it is reasonable to evaluate its effect on the results of a urinalysis. Few studies have investigated the association of PE with urinary tract symptoms and infections and have found an increased risk of urinary tract infection during the 2 months following a PE [6–8].

To our knowledge, the evaluation of PE as a possible contributory factor to transient MH in women has not been reported.

Materials and methods

After securing IRB approval, non-pregnant women > 18 years of age presenting to the gynecology private clinics in a tertiary care center were approached and consented to give a urine sample for analysis before and within an hour after PE. Women with known urinary tract disorders, gynecologic pathologies, suspected urinary tract infections, current vaginal bleeding, or within the first 3 days after the last day of menses, on anticoagulation therapy, or with a history of sexual intercourse in the past 24 h were excluded. Data collected included age and menopausal status.

Participants were asked to provide two mid-stream urine samples, one before PE and one after. Mid-stream urine samples were collected in standard urine containers, after properly cleansing the genitalia, as per the recommended method of collection by the European Confederation of Laboratory Medicine (ECLM) [9]. Samples were then labeled and directly taken to the laboratory for analysis.

The urine samples were processed in our laboratories using an automated urinalysis analyzer, the *Cobas 6500* (Roche, Germany), which undergoes daily quality control and is calibrated on a monthly basis. In our laboratory, results are reported as brackets depending on the number of RBCs/HPF: rare, [2–4], [4–6], [6–8], [8–10], [10–15], [15–20], and > 20. The latter is reported as “numerous RBCs.” In this study, brackets reported as “rare” or [2–4] were classified as no MH, while brackets \geq [4–6] were classified as MH.

McNemar test was used to evaluate the effect of PE on the prevalence of MH in women. Chi-square test was used to determine whether the conversion from no MH before PE to MH after PE is influenced by age or menopausal status. Age was divided into three categories: 18–35, 36–50, and > 50 years.

Statistical calculations were performed using SPSS 22.00 software, and $p < 0.05$ was considered significant.

Results

A total of 157 eligible participants were recruited. The mean age was 40 years ($20\text{--}53 \pm 9.0$); 127 (81%) were premenopausal (Table 1). Prior to PE, 13 (8.3%) had MH (Table 2).

Among 144 participants with no MH before PE, 22 (15.3%) had MH after PE.

Among 13 participants with MH initially, 5 women (38.0%) had no MH after PE.

Using the McNemar test, PE was found to significantly correlate with the conversion from no MH before PE to MH after PE ($p = 0.002$) (Table 2).

Chi-square test was used to analyze the impact of age on the conversion from no MH to MH following PE, and no statistical significance was found ($p = 0.451$). Similarly, the impact of menopausal status on the conversion from no MH to MH after PE was not found to be significant ($p = 0.411$).

When analyzing the change in brackets in the urinalysis of the 22 participants who had MH after PE, but not before, we found that 12 of 22 participants (55%) had a change of one bracket, i.e., from no MH to [4–6] RBC in urine. At the other end of the spectrum, two participants had a change from no MH to numerous RBCs in urine (six bracket difference) (Fig. 1).

Table 1 Sample distribution according to age and menopausal status ($N = 157$)

Demographics	<i>n</i> (%)
Age (years)	
18–35	66 (42.0)
36–50	62 (39.5)
> 50	29 (18.5)
Menopause	
Premenopausal	127 (80.9)
Postmenopausal	30 (19.1)

Table 2 Prevalence of microscopic hematuria before and after pelvic examination

	Microscopic hematuria <i>after</i> pelvic examination		Total
	No	Yes	
Microscopic hematuria <i>before</i> pelvic examination	No	22	144
	Yes	5	13
Total	127	30	157

Discussion

The prevalence of initial MH in our population (8.3%) is consistent with that reported by others [1]. The results of this study show that MH in women is more common following PE. Five women had MH before PE but not after, while 22 women had MH following PE but not before. The McNemar test is most appropriate to evaluate whether the conversion from no MH to MH is due to PE rather than chance. The McNemar associated p value of 0.002 confirmed the act of PE as a significant risk factor for MH.

One possible limitation of our study is that PE was not “uniform,” as it was performed by different practitioners. In addition, we did not differentiate whether the examination included any or a combination of the following: speculum examination (with or without Pap smear), digital examination, bimanual examination, and endovaginal ultrasound. The latter is frequently performed during gynecologic evaluation in our center. An ultrasound machine is present in all gynecology examination rooms, and the procedure carries minimal financial consequences. It is probable, however, that introducing a vaginal ultrasound probe is not more “traumatic” than

introducing a speculum in the vagina. Consequently, we believe that categorizing the pelvic examinations would not have materially changed the results. It is noteworthy that physicians were blinded to which participants were enrolled. This probably eliminated the possibility of PE “modification” that could have biased our results.

PE, regardless of the method used, involves vaginal manipulation and exerting pressure at the periurethral area and the bladder. It is conceivable therefore that microtrauma within the urethra or the bladder could lead to MH. The source of RBCs could also be mucosal microabrasions of the periurethral and vaginal areas. Irrespective of the exact reason, the fact remains that the urinalysis is reported as MH and may consequently trigger investigation.

There is evidence that “vaginal manipulation” or “vaginal expansion” such as sexual intercourse, and the presumably resultant minor localized trauma to the trigone and posterior bladder wall, increases the incidence of MH in women. In one study, 25% of asymptomatic women with no previous MH were found to have MH in the morning after sexual intercourse [10]. Another similar study showed that 73.3% of women were found to have MH immediately after sexual intercourse [11].

Exercise is also identified as one of the transient causes of MH because of several mechanisms, depending on exercise duration and intensity [12]. MH is a particularly common yet transient finding among long-distance runners. One study concluded that MH was present in 18% of urine samples collected from a group of male marathon runners directly after the race, but in none of the samples collected 24, 48 or 72 h after the race [13]. Another study involving female middle-distance track athletes also found MH in 12% of their urine samples immediately after exercise [14]. One of the proposed mechanisms of MH is bladder microtrauma from the repeated impact of the flaccid posterior bladder wall against its rigid and thick base [12]. It is possible that PE inflicts comparable trauma, albeit at a much smaller magnitude.

It is plausible to suspect that vaginal atrophy in menopause would increase the incidence of MH in women if the latter is actually due to vaginal manipulation such as PE. Notwithstanding the small number of postmenopausal women in our study (30), our results did not show a significant difference in conversion from no MH to MH between pre- and postmenopausal women ($p = 0.411$). It is noteworthy, however, that we did not capture the use of estrogen replacement in our postmenopausal women population.

We did not evaluate the status of bladder volume during each PE. This would constitute an interesting area to explore in future studies to determine whether PE after voiding actually affects the incidence of post-examination MH.

The change of only one bracket in RBC following PE in 12 of 147 (8.1%) remains a significant finding. Given that the frequently accepted upper limit of normal for urinary RBCs

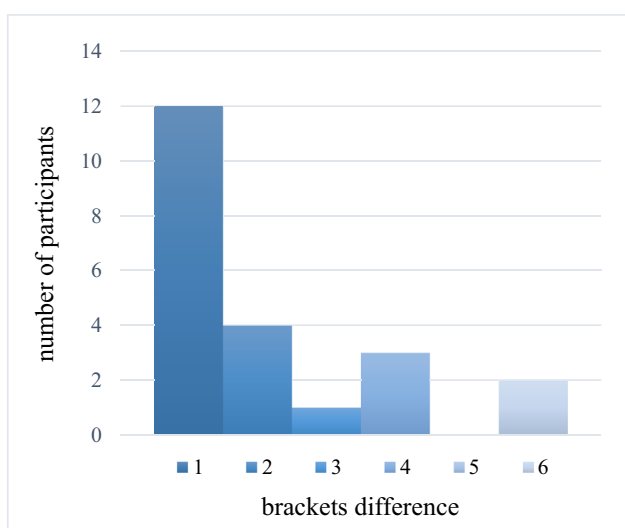


Fig. 1 Change in red blood cell brackets between the urinalysis results obtained before and after pelvic examination among participants who had microscopic hematuria after, but not before, pelvic examination

is 2 to 3 RBCs/HPF [3], this seemingly small change is clinically significant as it would have arguably triggered unnecessary investigation.

Among women who had initial MH, five women converted to no MH after PE. This could be explained by the intermittency of MH on urinalysis. In a home screening study, 231 patients with no identified cause of hematuria tested their urine weekly for a 3-month period, and 23 of them were found to have hematuria at least once [15].

In our study protocol, urinalysis was obtained within an hour following PE mostly for logistic purposes prior to the patient's discharge from the office. Consequently, one cannot estimate the incidence of MH if urinalysis is performed within a few hours or on the day following PE. Future studies could help in recommending an adequate time frame following which urinalysis would not reflect iatrogenic causes of transient MH.

Urinalysis is commonly ordered by gynecologists for screening for urothelial cancer or for other indications unrelated to urinary tract symptomatology. Not infrequently, women give urine samples for evaluation immediately following PE. Our study results suggest that in the absence of urinary symptoms, it is preferable not to perform a urinalysis immediately following PE.

In conclusion, PE can be an iatrogenic cause for MH regardless of age or menopausal status. Eliciting a history of PE may preclude the need for morbid and costly evaluation.

Compliance with ethical standards

Conflicts of interest None.

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