

Asymptomatic microscopic hematuria in women

Gisele Vissoci Marquini^{1*} , Sérgio Brasileiro Martins¹ , Letícia Maria Oliveira¹ ,
Márcia Maria Dias¹ , Claudia Cristina Takano¹ , Marair Gracio Ferreira Sartori¹ 

INTRODUCTION

Asymptomatic microscopic hematuria (AMH) is an important clinical sign of urinary tract malignancy. AMH has been variably defined over the years. It could be defined as three or more red blood cells per high-power field in the absence of infection as indicated in the American Urological Association (AUA) guidelines¹. The evidence is primarily based on the data related to male patients. However, whether the patient is a man or a woman influences the differential diagnosis of AMH, and the risk of urinary tract malignancy (e.g. bladder, ureter, and kidney) is significantly less in women than in men^{1,2}.

Among women, being older than 60 years, having a history of smoking, and having gross hematuria are the strongest predictors of urological cancer. In low-risk, never-smoking women younger than 50 years without gross hematuria and with fewer than 25 red blood cells per high-power field, the risk of urinary tract malignancy is £0.5%¹⁻³.

Although AMH has a clinical importance, the research on women in this area has been limited. It is incumbent on the experts in the field of female pelvic medicine to advance the science and develop management algorithms for AMH in women⁴.

Faced with this situation, the objective of this study was to review the literature to identify the recommended guidelines about how to approach AMH in women.

METHODS

Search strategy

This study was performed by a qualitative review.

Selection criteria

All of the publications indexed in Medline (PubMed), LILACS, and BIREME databases in August 2020 were searched using the key words "hematuria," "guideline(s)," and "women."

Data collection and analysis

Following this search strategy, a total of 14 articles were included in this study. Out of 14 studies, 11 commented on recommendations and best strategies to approach this sign in women. Three studies were excluded because of their different objectives (i.e. two of them have studied urinary tract infection in women and the other interstitial cystitis/painful bladder syndrome). Another study has been included in a quote of teaching form for the citation of causes of AMH.

RESULTS AND DISCUSSION

It is estimated that about two-third of the women with hematuria in one examination will not present in another during the lifetime, since menstruation, fever, infection, injury of the urinary tract, and physical exercise are the main causes for this contamination⁵.

According to Richter et al., the risk factors for AMH in women are smoking, a history of pelvic radiation, and a history of nephrolithiasis⁶. When stratifying the quantity of AMH, women with increased red blood cells per high-power field were more likely to have significant findings on their imaging results⁶.

Medical history followed by the physical examination is the initial step to assess hematuria. Subsequently, a distinction should be made between glomerular and non-glomerular hematuria. This can be achieved by a search of red blood

¹Universidade Federal de São Paulo, Department of Gynecology – São Paulo (SP), Brazil.

*Corresponding author: giselemarquini@gmail.com

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cell casts or dysmorphic cells. The main causes of glomerular hematuria in women are as follows: immunoglobulin A (IgA) nephropathy, thin glomerular membrane disease, and hereditary glomerulonephritis⁵.

Malignant neoplasia, nephrolithiasis, cystitis, urethritis, and other causes of non-glomerular bleeding can be diagnosed by imaging examination. To evaluate lithiasis, the computed tomography (CT) should be utilized with or without radiocontrast, respectively. Patients with risk factors for bladder cancer should be performed a urinary cytology test or undergo a cystoscopy. Other less frequent causes of hematuria can be investigated depending on the clinical indications⁵.

A practical guideline for general practice for imaging of the urinary tract in adults has suggested that ultrasound should be chosen in patients with microscopic hematuria (MH) and nonspecific abdominal pain. The CT should be used in cases with nonspecific findings using urography and ultrasound⁷.

In 2012, the AUA released a revision of the AMH guidelines for postmenopausal women. That study population included 237 women with a mean \pm SD age of 67.1 \pm 8.3 years. In postmenopausal women evaluated for AMH, the overall prevalence of urinary tract malignancy was low at 1.4%⁸.

The AUA cited that future directions should include continued research into the confounding risk factors for AMH in postmenopausal women such as vaginal atrophy, pelvic organ prolapse, and recurrent urinary tract infection. Investigation on the exact correlation of urinary dipstick to microscopic urinalysis may also be a way to decrease the number of unnecessary and costly evaluations if definitive evidence shows that trace blood is not associated with AMH⁸.

On the contrary, the prevalence of AMH is greater in postmenopausal women (i.e., about 20%) than that in the general population, presumably due to the same risk factors such as pelvic organ prolapse or vaginal atrophy^{8,9}. Cystoscopy, renal function testing, and CT urography are now recommended after one positive urinalysis, regardless of gender or the presence of prolapse. Due to the low incidence of urological malignancy detected as well as the increased prevalence of MH found in women with prolapse, specific guidelines for the management of MH in this population are needed⁹.

Limitations may difficult the analysis of AMH in women. The proper evaluation and treatment options are understudied in females^{4,10,11}. While urinalysis remains a common diagnostic tool, most cases of both MH and gross hematuria are not fully evaluated according to the guidelines. The use of cystoscopy,

cytology, and upper tract imaging is limited¹⁰. Besides, the guidelines recently updated by the AUA for the evaluation of AMH are based on the data derived predominantly from men. AMH in women requires separate guidelines^{4,10,11}.

In addition, although gross hematuria is a relatively uncommon condition in general obstetrics and gynecology practice, MH is a common incidental finding during routine antepartum or other gynecological visits¹⁰. Pregnancy, menstruation, and vaginal atrophy increase the number of potential false diagnoses¹⁰. Probably, due to these factors, unfortunately women are less likely to be referred to urology or urogynecology, and also women wait longer than men for review and diagnosis of bladder cancer¹².

CONCLUSIONS AND RECOMMENDATIONS

The American College of Obstetricians and Gynecologists and the American Urogynecologic Society encourage organizations producing future guidelines on the evaluation of MH to perform sex-specific analysis of the data and produce practical sex-specific recommendations¹.

In the meantime, the American College of Obstetricians and Gynecologists and the American Urogynecologic Society recommend that asymptomatic, low-risk, never-smoking women aged 35–50 years undergo evaluation only if they have more than 25 red blood cells per high-power field¹.

Among women, being older than 60 years, having a history of smoking, and having gross hematuria are the strongest predictors of urological cancer¹. Faced with this scenario, this review may encourage and provide evidence for future guidelines on AMH in women.

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AUTHORS' CONTRIBUTIONS

GVM: Data curation, Writing – review & editing. **SBM:** Data curation, Writing – review & editing. **LMO:** Data curation, Writing – review & editing. **MMD:** Data curation, Writing – review & editing. **CCT:** Data curation, Writing – review & editing. **MGFS:** Conceptualization, Formal Analysis, Writing – review & editing.

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