

Patients with microscopic and gross hematuria: practice and referral patterns among primary care physicians in a universal health care system

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Abstract

Background: Hematuria is one of the most common findings on urinalysis in patients encountered by primary care physicians. In many instances it can also be the first presentation of a serious urological problem. As such, we sought to evaluate current practices adopted by primary care physicians in the workup and screening of hematuria.

Methods: Questionnaires were mailed to all registered primary care physicians across Quebec. Questions covered each physician's personal approach to men and postmenopausal women with painless gross hematuria or with asymptomatic microscopic hematuria, as well as screening techniques, general knowledge with regards to urine collection and sampling, and referral patterns.

Results: Of the surveys mailed, 599 were returned. Annual routine screening urinalysis on all adult male and female patients was performed by 47% of respondents, regardless of age or risk factors. Of all the respondents, 95% stated microscopic hematuria was associated with bladder cancer. However, in an older male with painless gross hematuria, only 64% of respondents recommended further evaluation by urology. On the other hand, in a postmenopausal woman with 2 consecutive events of significant microscopic hematuria, only 48.6% recommended referral to urology. Findings were not associated with the gender of the respondent, experience or geographic location of practice (urban vs. rural).

Interpretation: There seems to be reluctance amongst primary care physicians to refer patients with gross or significant microscopic hematuria to urology for further investigation. A higher level of suspicion and further education should be implemented to detect serious conditions and to offer earlier intervention when possible.

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Résumé

Contexte : L'hématurie est l'une des observations les plus courantes lors des analyses d'urine signalées par les médecins de soins primaires. Souvent, elle peut aussi être le premier signe d'un problème urologique grave. Nous avons donc voulu évaluer les pratiques actuelles des médecins de soins primaires dans le dépistage et l'évaluation de l'hématurie.

Méthodologie : Des questionnaires ont été envoyés à des médecins de soins primaires au Québec. Les questions portaient sur l'approche personnelle des médecins dans les cas de femmes ménopausées et d'hommes présentant une hématurie macroscopique sans douleur ou une hématurie microscopique asymptomatique, et sur les techniques de dépistage, les connaissances générales concernant la collecte et l'évaluation des échantillons d'urine, et les tendances quant à l'orientation vers un spécialiste.

Résultats : Sur tous les questionnaires envoyés, 599 nous ont été retournés. Une analyse d'urine annuelle systématique de tous les hommes et femmes adultes était réalisée par 47 % des répondants, peu importe l'âge du patient ou ses facteurs de risque. Sur tous les répondants, 95 % ont indiqué qu'une hématurie microscopique était associée à un cancer de la vessie. Cependant, chez les hommes âgés présentant une hématurie macroscopique sans douleur, seulement 64 % des répondants recommandaient une évaluation plus poussée par un urologue. En revanche, chez les femmes ménopausées présentant une hématurie microscopique significative lors de 2 évaluations consécutives, seulement 48,6 % des répondants ont recommandé de consulter un urologue. Les résultats n'ont pas été associés au sexe du répondant, ni à son niveau d'expérience ou la situation géographique de son cabinet (région urbaine ou rurale).

Interprétation : Les médecins de premier recours semblent réticents à diriger vers un urologue pour des examens plus approfondis les patients présentant une hématurie macroscopique ou une hématurie microscopique significative. Il faut encourager les médecins de soins primaires à être plus vigilants et il faut leur transmettre plus d'information afin qu'ils soient en mesure de dépister des maladies graves et d'offrir plus rapidement une intervention dans la mesure du possible.

Introduction

Hematuria is one of the most common findings on urinalysis in patients encountered by general practitioners (GPs), with an incidence of 4 per 1000 patients per year;¹ it represents about 6% of new patients seen by urologists.² The source of hematuria can be anywhere along the urinary tract and could be the first presentation of a serious condition including malignancy. The Canadian Urological Association (CUA) defines hematuria as greater than 2 red blood cells/

Table 1. A sample of clinical vignettes and questions from the survey

1. A 45-year-old man presents to you with painless gross hematuria and a negative urine culture. He was treated with a 10 day course of ciprofloxacin and hematuria resolved. He comes to you in follow-up 2 weeks later and is asymptomatic. What would you do? You may select >1 answer.

- Refer to nephrology
- Reassure and follow-up with urinalysis in 6 months
- Repeat urine culture
- Order urinalysis
- Refer to a urologist

Only 64% of GPs would refer this patient to urology.

2. A 55-year-old postmenopausal lady has had asymptomatic microscopic hematuria (6 RBC/hpf) in midstream urine collection when she was seen on 2 occasions 6 months apart. What would you recommend? You may select >1 answer.

- Refer to nephrology
- Abdominal ultrasound
- Pap smear
- Refer to a urologist
- Reassure and follow-up in 6-12 months
- Other, please explain

Only 49% of GPs would refer this patient to urology.

3. For what types of patients do you typically order routine screening urinalyses during routine physical check-ups? You may select >1 answer

- All patients
- Men only
- Women only
- Smokers only
- Age >50 years
- Never routinely

Around 47% of GPs perform routine screening urinalyses on all men and women regardless of risk factors (such as smoking history).

4. What can microscopic hematuria in a midstream urine sample be associated with? You may select >1 answer.

- UTI
- Kidney stones
- BPH
- Prostate cancer
- Bladder cancer
- Uterine fibroid
- Normal variant

Around 95% of GPs correlated microscopic hematuria with bladder cancer.

5. What would you consider significant microscopic hematuria in 2 midstream urine collections?

- ≥1 RBC/ hpf
- ≥3 RBC/ hpf
- ≥10 RBC/ hpf
- ≥20 RBC/ hpf
- ≥50 RBC/ hpf
- ≥100 RBC/ hpf

Over 50% of GPs were unable to correctly quantify significant microscopic hematuria.

RBC/HPF: red blood cells/high power field; UTI: urinary tract infection; BPH: benign prostatic hyperplasia; GPs: general practitioners.

high power field (RBC/hpf) on 2 separate urinalyses in the absence of exercise, menses, sexual activity or instrumentation.³ Similarly, the American Urological Association (AUA) defines it as 3 or more RBC/ hpf in 2 of 3 properly collected urinalysis specimens.⁴

It is understood that gross hematuria should be investigated. Although the yield of finding pathology in patients with asymptomatic microscopic hematuria is lower than those with gross hematuria, there are clear and established guidelines for its workup. In 2 population-based studies, RBCs were documented in the urine of 9% to 18% of asymptomatic adults.^{5,6} Evidence shows that up to 13% of patients with hematuria end up being diagnosed with a urologic cancer and up to 53% of those considered initially to have benign conditions end up having urologic malignancies.^{7,8} As such, we sought to shed light on the current practices adopted at the primary care level in the workup and screening of hematuria in a universal health care system.

Methods

From September 2008 to January 2009, a questionnaire was mailed in both French and English to registered GPs in the province of Quebec. Physicians included in the mailing list were all those who were registered as family physicians or general practitioners. The survey consisted of multiple choice questions preceded by an explanation of the purpose of the study, as well as a stamped self-addressed return envelope. Some questions required only one answer while others gave the respondents the choice to select as many answers as they felt appropriate. The identity of the respondents was kept completely anonymous and no attempt was made to track non-respondents.

The first 2 questions were clinical case scenarios which covered each physician's personal approach to older men with painless gross hematuria and postmenopausal women with asymptomatic microscopic hematuria. These questions were followed by questions relating to screening techniques and general knowledge with regards to urine collection, sampling and interpretation of results.

Bivariate analysis (χ^2 test of association) was used to examine relationships between hematuria questions and years of medical practice, area of medical practice and physician gender.

Results

Surveys were mailed to all GPs in Quebec and 599 were completed and returned (15.7% response rate). Of these 599 surveys, 141 were not included in the analysis due to reasons including retirement, GP caring for pediatric and/or women only population or having solely administrative functions. With regards to the profile of remaining respon-

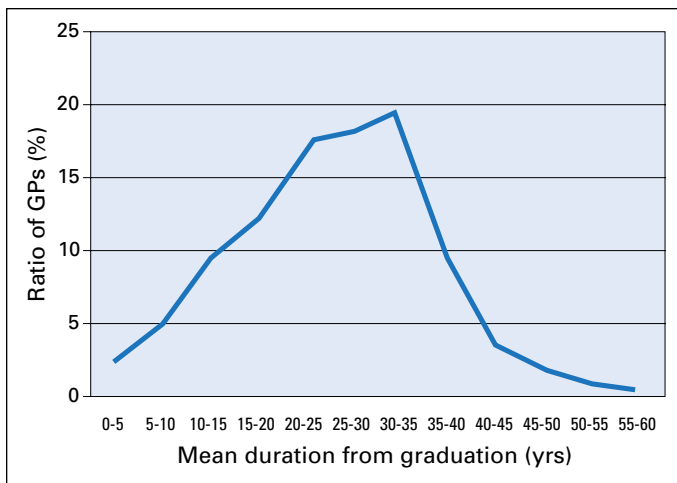


Fig. 1. Mean years from graduation of general practitioners.

dents ($n = 458$), there were 256 (56%) males, and 202 (44%) females, and the overall mean years from graduation was 24.8 years (median = 25, range 3-58) (Fig. 1). No significant difference was noted between the younger and older cohorts of respondents in this study with regards to response rate (8.1% and 7.3% response rates for less and more than 25 years of practice, respectively, $p = 0.78$).

Screening urinalysis with the annual physical examination was considered routine for all patients in 46.7% of GPs and was not performed, regardless of the patients' age and smoking history, by 26% of GPs. The definition of significant microscopic hematuria on 2 consecutive urine samples was noted correctly by only 42.1% of respondents. Most respondents (50.3%) stated significant microscopic hematuria as >10 RBC/hpf. Respondents were then proposed several scenarios. In an older male with painless gross hematuria and negative urine culture, only 63.7% of GPs recommended further evaluation by urology. On the other hand, in a 55-year-old postmenopausal woman with 2 consecutive events of significant microscopic hematuria, only 48.6% recommended referral to urology. This was despite the fact that when asked about what was associated with microscopic hematuria, 94.6% of GPs responded bladder cancer. The other common answers included urinary tract infections (UTI) and kidney stones in more than 90% of returned surveys (Fig. 2).

Using a student's t -test, the results were further analyzed to account for different GP demographics. When physicians were stratified depending on their time from graduation (0-10 years, 11-20 years, 21-30 years, 31-40 years and 41-50 years) no significant differences were observed ($p = 0.6$). Similarly, no difference in results was noted when stratifying the physicians according to gender ($p = 0.93$). Finally, there was a statistically insignificant trend ($p = 0.09$) towards more referral to urology in urban versus rural areas of practice

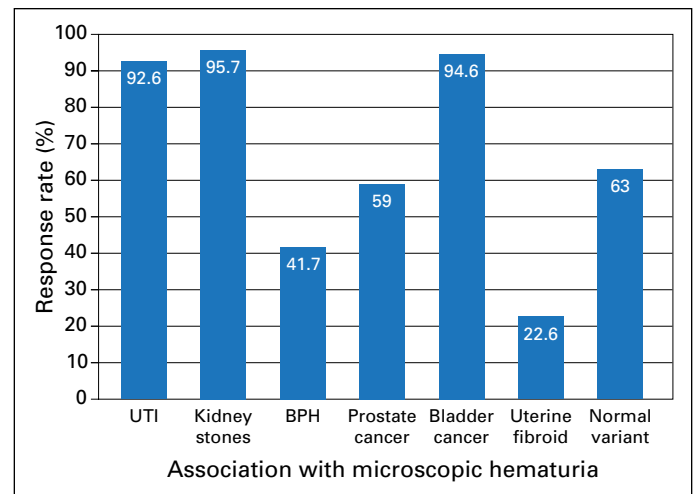


Fig. 2. Answers to the question: What is microscopic hematuria in a midstream urine sample associated with?

for both macroscopic (68% vs. 58%) and significant microscopic hematuria (51.1% vs. 44.4%).

Discussion

In this study, we observed a significant reluctance amongst primary care physicians in a universal health care system to refer patients with gross or significant microscopic hematuria to urology for further investigation.

There is consensus amongst experts that gross hematuria is a worrisome presentation and warrants a thorough investigation.^{3,7-10} This certitude stems from strong evidence associating it with urologic malignancies. In fact, visible blood in the urine is thought to be the first presentation in 85% and 40% of patients with bladder and renal cancers, respectively.⁸ As such, in this setting, both the CUA and AUA recommend thorough physical examination, upper tract imaging with computerized tomography (CT), intravenous urography (IVU) or renal ultrasound, as well cytology and cystoscopic examination.^{3,4}

With that in mind, our first goal was to investigate how GPs would approach a patient with macroscopic hematuria and presented the case of a 45-year-old man with resolved asymptomatic gross hematuria and no evidence of infection. We were surprised to see that only 63.7% of the respondents elected to refer to urology for full investigation. Notably, this rate is similar to ones obtained from another recent large multi-institutional questionnaire emanating from the United States with only 69% and 77% of physicians from 2 different centres electing to refer to urology in the face of gross hematuria.¹¹ As such, one conclusion that could be extracted from this is that there seems to be a generally relaxed attitude and/or lack of knowledge with regards to referring and fully evaluating patients with gross hematuria. Another potential explanation could be the difficult access to

specialists in Quebec, thus discouraging GPs from referring to urology. This approach is concerning and may possibly lead to delays in diagnosis and initiation of therapy for potentially serious conditions.

We then chose to shift our attention to the more common scenario of asymptomatic microscopic hematuria and its management. The challenge here is to detect the more serious conditions while minimizing the costs and morbidity of unnecessary investigation. This is particularly true when one keeps in mind that in retrospective studies, an overall prevalence rate for microscopic hematuria as high as 13% in the general population has been reported.¹² As such, while there is a need for risk stratification to appropriately detect worrisome patients, there still remains an elevated chance of malignancy with microscopic hematuria. Referral studies have shown that up to 26% of high-risk patients with hematuria harbour genitourinary malignancies.¹³ Even in low-risk cases, 4% of patients with asymptomatic microscopic hematuria are found to have bladder cancer.¹⁴ The need for early detection in these patients is further illustrated by the fact that 92% of cancers detected during the workup of hematuria are still localized and curable.¹⁵ Accordingly, best practice guidelines were put forth by the European Association of Urology, CUA and the AUA. In the absence of external factors or evidence of glomerular source, the AUA guidelines recommend upper tract imaging, cystoscopy and cytology in all adult patients.⁵ The CUA has slightly varied guidelines with immediate urine cytology collection and cystoscopy alongside initial upper tract imaging (renal ultrasound) in all patients over 40 years old or if risk factors are present regardless of the patient's age.³

To evaluate GP practice patterns in this population of patients with significant microscopic hematuria and to assess any gender disparity among GP evaluation, we presented a clinical scenario of a postmenopausal woman with 2 episodes of clear asymptomatic microscopic hematuria. We were also surprised to see that only 48.6% of GPs elected for referral to urology for further investigation. These results, though low, were still an improvement over the referral rates in the previously reported American-based questionnaire (36% referral to urology for microscopic hematuria).¹¹ One may argue that the reluctance to refer to urology may stem from lack of knowledge about the association between hematuria and genitourinary malignancy at the primary care level; however, this is not the case in this study as >90% of respondents stated that microscopic hematuria was associated with bladder cancer. The disparity between the referral rates within the 2 above-mentioned clinical scenarios may be due to multiple factors. For example, the level of suspicion may be higher when evaluating patients with gross hematuria compared to microscopic hematuria; similarly, the level of suspicion of serious urologic conditions may also be higher at the primary care level when evaluating male

versus female patients who present with hematuria. This finding is supported by several studies showing significant delay in diagnosis and workup in females who present with hematuria when compared to male.⁶

Another possibility for this reluctance to refer or workup microscopic hematuria seems to be related to how GPs define and quantify *significant* microscopic hematuria. Whether one opts to follow the AUA or CUA guidelines, most would agree that the upper limit of normal for the presence of RBC in urine is 2 RBC/HPF.^{3,4} Also, emphasis is placed on the fact that there is no safe value for microscopic hematuria to safely rule out transitional cell carcinoma.¹⁶ Our survey showed that over half of the GPs considered ≥ 10 RBC/hpf to be significant with only 42.1% correctly answering ≥ 3 RBC/hpf. Clearly, the need for hematuria education seems to extend to basic concepts which are essential for accurate diagnosis and treatment.

Finally, we asked the physicians who they would consider screening with a urinalysis on a routine physical check-up. Around half of the respondents perform routine screening urinalysis on all men and women regardless of risk factors (such as smoking history or occupation exposure to chemicals). This was surprising since the American Cancer Society, the AUA and the CUA do not currently recommend routine screening urinalysis. Furthermore, the US Preventive Services Task Force and the Canadian Task Force on the Periodic Health Examination both recommend *against* doing so in the face of insufficient evidence.^{3,4,17-19}

We believe this project to be a very helpful tool in the assessment of general practice with regards to diagnosis, workup and management of a very common urologic presentation, such as hematuria. Clearly, further education needs to be implemented at the primary care level to correct deficiencies, prevent delays in diagnosis, and improve care.

Conclusions

Routine screening urinalyses are being over used by GPs in the absence of clear indications. There is reluctance amongst primary care physicians to refer patients with gross or significant microscopic hematuria to urology for further investigation. A higher level of suspicion should be advocated and further education should be instilled at the primary care level to avoid delays in the detection of serious conditions and to offer earlier intervention when possible.

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Competing interests: The cost of the survey (printing, stamps and mailing) was covered by an unrestricted educational grant from GlaxoSmithKline. All remaining aspects of this study were conducted at the discretion of the authors.

This paper has been peer-reviewed.

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