Genitourinary malignancy among patients presenting with microscopic hematuria in Northwestern Ontario

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ABSTRACT

INTRODUCTION: Microscopic hematuria (MH) may indicate an underlying genitourinary (GU) malignancy. Accordingly, MH workup is essential to mitigate GU cancer-related morbidity and mortality. This study aimed to evaluate the etiologies of MH in Northwestern Ontario, Canada.

METHODS: We conducted a retrospective cohort chart review of 2545 patients referred to our institution for MH from 2010–2020. Demographic and clinical data were collected. Low- and high-grade MH were defined as ≤25 and >25 red blood cells (RBCs) per high-power field (HPF), respectively.

RESULTS: The prevalence of GU cancer was 5.2% among patients with MH; the majority of cases (108/133, 81.2%) were identified during the initial workup, with urothelial carcinoma of the bladder being the most common subtype (81.2%). GU cancer was significantly associated with male sex (odds ratio [OR] 2.958, p<0.001), older age (OR 1.033, p<0.001), history of gross hematuria (GH) occurring more than 12 months prior (OR 3.469, p<0.001), prior lower urinary tract symptoms (LUTS, OR 0.081, p=0.014), and high-grade MH (>25 RBC/HPF, OR 2.977, p<0.001). High-grade GU cancer was significantly associated with male sex (OR 3.012, p<0.001), older age (OR 1.033, p<0.001), prior GH (OR 4.195, p<0.001), and history of LUTS (OR 0.088, p=0.016).

CONCLUSIONS: In our cohort, the prevalence of GU malignancy among patients with MH was 5.2%. Significant associations were observed with male sex, older age, and prior GH. High-grade MH was linked to increased GU cancer risk, emphasizing the importance of followup even in patients with low-grade MH, with prioritization given to those with high-grade MH.

INTRODUCTION

Microscopic hematuria (MH) is defined as the presence of ≥3 red blood cells (RBCs) per high-power field (HPF) on urine microscopy, according to the Canadian Urological Association (CUA) and the American Urological Association (AUA)/Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU) guidelines.[1,2]

MH may signify various underlying conditions, including malignancies,[3-9] highlighting the need for comprehensive evaluation to reduce associated morbidity and mortality. According to the AUA/SUFU guidelines, initial workup for MH includes a history, physical examination, renal function tests, and imaging to assess risk factors for genitourinary (GU) malignancies and exclude non-malignant, non-renal causes. Subsequent steps include determining whether hematuria is glomerular or non-glomerular in origin and considering referral to nephrology or urology.[10]

This discretionary approach may compromise the effectiveness of the recommended MH workup, particularly in regions facing resource constraints. Canadian studies have highlighted provincial variations in adherence to these guidelines, with some regions demonstrating strong compliance,[11] while others face challenges due to unique geographical, ethnic, and economic factors.[12] The issue is further complicated by the financial implications of unnecessary evaluations, as MH is commonly linked to urinary tract infections (UTIs) or gynecologic causes,[13-20] and by racial disparities in GU can-

KEY MESSAGES

- In our study, the prevalence of GU cancer in patients with microscopic hematuria (MH) was 5.2%.
- Male sex, older age, prior gross hematuria, and high-grade MH were significantly associated with GU cancer.
- The incidence of new GU malignancies following a negative workup was 1.4%, similar to rates of incidental findings on imaging in the general population.
- Results emphasize the need for long-term followup in patients with MH, even when initial evaluation is negative.

cer risk,[21-23] which may influence guideline adherence among primary care physicians. Moreover, diagnostic delays may lead to tumors being detected at a more advanced stage. Recommended benchmarks are 12 weeks for high-grade and six months for low-grade tumors.[24]

Northwestern Ontario (NWO) is hypothesized to face challenges in MH workup due to rural geography, healthcare disparities, and cultural barriers, compounded by prior gaps in cancer care.[25,26] This study aimed to evaluate the prevalence and etiologies of MH in NWO using medical records from Thunder Bay Regional Health Sciences Centre (TBRHSC).

METHODS

Study design

We conducted a retrospective cohort study of patients referred to our institution for MH evaluation between 2010 and 2020. The study was approved by the TBRHSC's Research Ethics Board (REB #2020502). The requirement for informed consent was waived by the REB due to the retrospective nature of the study.

Study participants

Patients aged ≥35 years with MH (≥3 RBC/HPF on urinalysis) and a minimum followup of six months were included. Exclusion criteria were concurrent UTI, concurrent urolithiasis that did not require further evaluation, prior urogenital malignancy, gross hematuria (GH) within the preceding 12 months or GH occurring more than 12 months prior to enrollment without a documented negative workup, and the presence of GU foreign bodies. The sample size was determined using the standard formula for estimating proportions,[27] based on a malignancy prevalence of 3%, with type I and II error rates of 5% and 20%, respectively: $N=[Z^2\times p(1-p)]/E^2$, where Z is the Z-score for the desired confidence level, p is the estimated proportion, and E is the margin of error. This yielded a minimum sample size of 1071 patients.

Data collection and cancer classifications

Data for this study were extracted from electronic medical records (EMRs) of patients evaluated at the hospital and affiliated urology clinics. Collected variables included demographic characteristics (sex, age, body mass index [BMI], and residential postal code), medical history (hypertension, diabetes mellitus, prostate cancer [PCa], urothelial carcinoma, hematuria, nephrolithiasis, and lower urinary tract symptoms [LUTS]), chronic analgesic use, and prior abdominopelvic radiation or chemotherapy. For this study, LUTS was considered present when a documented history of storage or voiding complaints (e.g., frequency, urgency, nocturia, hesitancy, weak stream) was noted in the EMR. Chronic analgesic use referred to patients with documented continuous use of non-steroidal anti-inflammatory drugs or acetaminophen for at least three months. Social history, including smoking status (current or former smoker vs. non-smoker), was also collected.

In this study, GU cancers were classified according to the 2016 WHO classification system,[28] and were subsequently grouped as high- or low-grade for analysis. High-grade cancers included high-grade urothelial carcinoma, muscle-invasive bladder cancer, squamous cell carcinoma, adenocarcinoma, small cell carcinoma, and carcinoma in situ of the bladder; clear-cell renal carcinoma, papillary renal carcinoma type 2, collecting duct carcinoma, and medullary carcinoma of the kidney; high-grade urothelial carcinoma, squamous cell carcinoma, and adenocarcinoma of the ureter; and high-grade prostate adenocarcinoma. Low-grade cancers included low-grade urothelial carcinoma and papillary urothelial neoplasm of low malignant potential of the bladder; papillary renal cell carcinoma type 1, chromophobe renal cell carcinoma; low-grade urothelial carcinoma of the ureter; and low-grade prostate adenocarcinoma.

Low- and high-grade MH were defined as ≤25 and >25 RBCs/HPF, respectively. The highest RBC/HPF

Table 1. Comparison of clinical and demographic variables between non-cancer and cancer groups

	Non-cancer	Cancer	p
Number of patients	2,412 (94.8)	133 (5.2)	-
Sex (male:female ratio)	1:1.42	1:1.77	<0.001*
Age, years, mean (SD)	50.5 (14.2)	58.5 (10.7)	<0.001*
Prior GH (>12 months with negative workup), n (%)	169 (7)	33 (24.8)	<0.001*
Smoking status, mean score (SD)	1.14 (0.35)	1.11 (0.31)	0.34
Obesity, n (%)	96 (4)	9 (6.8)	0.067
MH grade (>25:≤25 RBC/HPF), n (%)	1037 (43)	74 (55.6)	0.029*
Prior LUTS, n (%)	265 (11)	1 (0.8)	<0.001*
Family history of GU cancer, n (%)	145 (6)	11 (8.3)	0.323
Prior abdominopelvic radiation, n (%)	48 (2)	7 (5.3)	0.003*
Prior chemotherapy, n (%)	48 (2)	5 (3.8)	0.07
Chronic analgesic use, n (%)	48 (2)	3 (2.3)	0.789
Family history of genetic disorders, n (%)	24 (1)	4 (3)	0.152
Personal history of genetic disorders, n (%)	24 (1)	4 (3)	0.137

*Significant relationship. GH: gross hematuria; GU: genitourinary; HPF: high power field; LUTS: lower urinary tract symptoms; MH: microscopic hematuria; RBC: red blood cell.

value from available urinalysis reports was used for analysis. A minimum followup period of six months was required. Subsequent evaluations (repeat cystoscopy, imaging, or urinalysis) were performed at the discretion of the treating urologist based on the patient's risk profile and persistence of hematuria.

Statistical analysis

Continuous variables were assessed for normality using the Kolmogorov-Smirnov test and summarized as means and standard deviations. Categorical variables were summarized as frequencies and percentages. Group comparisons for continuous variables were performed using one-way ANOVA assuming equal variances; for two-group comparisons, this was equivalent to an independent samples t-test. Categorical variables were compared using the Chi-squared test. Risk factors for GU cancer were evaluated using generalized linear models, with results reported as odds ratios (OR) and 95% confidence intervals (CI). Statistical significance was defined as a two-sided $p<0.05$.

Missing data were handled by calculating the mean proportion of missing values per variable. Missing data were assumed to be missing completely at random, with no variable exhibiting more than 5% missingness. Therefore, multiple imputation by chained equations was applied. All analyses were performed using R software (version 4.2.3).

RESULTS

Patient demographics and baseline characteristics

A total of 2545 patient records were reviewed; 1443 were female (56.7%). The mean age was 51.3±14.1 years. Of the 1196 patients who underwent microscopic urinalysis, the majority (1077, 90.1%) demonstrated low-grade MH (3–25 RBCs/HPF). The most common findings in the social and medical history were hypertension (880, 34.6%) and smoking (742, 29.2%). These were followed by a history of LUTS (274, 10.8%) and prior GH (192, 7.5%). On average, patients resided 68.1±137.1 km from their urology service provider. Table 1 summarizes demographic variables between the non-cancer and cancer groups.

Characteristics of patients with and without GU cancer

The most common finding during workup was the absence of pathologic abnormalities (76.9%). Malignancy was identified in 133 patients (5.2%), with high prevalence among the high-grade MH (>25 RBC/HPF) group 12.6% vs. 4.4% in the low-grade MH (≤25 RBC/HPF). Of the 133 malignancies, 108 (81.2%) were diagnosed at baseline evaluation, with the remainder identified during followup. Among these, the most frequent diagnosis was urothelial carcinoma of the bladder (108, 81.2%), followed by renal carcinoma (14, 10.5%), upper tract urothelial carcinoma (6, 4.5%), and PCa (5, 3.8%).

Patients in the cancer group had a significantly higher mean age (58.5±10.7 years) compared to those in the non-cancer group (50.5±14.2 years, $p<0.001$). Significant differences were also observed in sex ($p<0.001$), prior abdominopelvic radiation exposure ($p=0.003$), prior GH >12 months ($p<0.001$), prior LUTS ($p<0.001$), and MH-grade based on the >25 RBCs/HPF cutoff ($p=0.029$). There was no significant difference in mean distance from the provider between the cancer and non-cancer groups ($p=0.392$).

Findings from initial evaluation and followup

Table 2 summarizes the initial and followup findings of the patients. Initial workup demonstrated non-malignant pathology in 18.9% and malignancy in 4.2% of patients. The most common cancer diagnosis was

urothelial carcinoma of the bladder (3.5%), followed by renal carcinoma (0.4%), upper tract urothelial carcinoma (0.2%), and PCa (0.1%).

Among the 1812 patients monitored for ≥3 years, 25 new malignancies (1.4%) were diagnosed despite a previously negative initial workup, as follows: urothelial carcinoma of the bladder (20, 1.1%), renal carcinoma (3, 0.2%), and PCa (2, 0.1%). Based on followup findings, 59 patients who initially presented with low-grade MH (≤25 RBC/HPF) were diagnosed with cancer. Of these, 39 (two-thirds) were found to have cancer during the initial workup, while the remaining 20 (one-third) were diagnosed during the followup period.

GU cancer risk factors

Overall, 81.2% of the cohort was diagnosed at initial presentation. Multivariable logistic regression analysis (Table 3) identified several significant independent factors associated with GU malignancies. These included male sex (OR 2.958, p<0.001), increasing age (OR 1.033, p<0.001), prior GH >12 months (OR 3.469, p<0.001), prior LUTS (OR 0.081, p=0.014), and high-grade MH (>25 RBC/HPF; OR 2.977, p<0.001).

For high-grade malignancies, male sex (OR 3.012, p<0.001), older age (OR 1.033, p<0.001), and prior GH >12 months (OR 4.195, p<0.001) emerged as independent risk factors. In contrast, a previous history of LUTS was associated with a low probability of high-grade cancers (OR 0.088, p=0.016).

DISCUSSION

MH is a common clinical finding with a broad differential diagnosis, ranging from benign causes, such as UTIs and lithiasis, to serious conditions, including GU malignancies.[3-9] Although often asymptomatic and incidentally detected on routine urinalysis, its clinical significance remains a subject of ongoing debate.

Our study highlights the diagnostic yield and risk factors for GU malignancies among patients with MH in NWO. We observed a 5.2% malignancy rate, reflecting a substantial cancer burden in this population. Urothelial carcinoma of the bladder was the most common diagnosis, accounting for 81.2% of cases, followed by renal carcinoma (10.5%), upper tract urothelial carcinoma (4.5%), and PCa (3.8%). The prevalence of GU cancer was higher in the high-grade MH group (>25 RBC/HPF) at 12.6% compared to 4.4% in the low-grade MH group (≤25 RBC/HPF).

In their population-based study, Nørgaard et al evaluated 134 173 patients within three months of a MH and GH diagnosis.[29] Among these patients, 1.9% were diagnosed with muscle-invasive bladder cancer, 0.8% with non-muscle-invasive bladder cancer, 0.4% with renal carcinoma, and 1.1% with PCa. The cumulative incidence (absolute risk) of any cancer diagno-

Table 2. Most probable causes of microscopic hematuria at initial evaluation and during followup

Pathology/most probably cause of MH	n (%)
Initial evaluation	
No pathology	1956 (76.9)
Non-cancer pathology	481 (18.9)
Urothelial carcinoma of bladder	88 (3.5)
Renal carcinoma	11 (0.4)
Upper tract urothelial carcinoma	6 (0.2)
Prostate cancer	3 (0.1)
6-month followup	
Urothelial carcinoma of bladder	3 (50.0)
Stones GU tract	1 (16.7)
Prostate cancer	1 (16.7)
Other benign causes	1 (16.7)
12-month followup	
Urothelial carcinoma of bladder	5 (25.0)
Stones GU tract	5 (25.0)
Other benign causes	10 (50.0)
24-months followup	
Urothelial carcinoma of bladder	9 (17.6)
Renal carcinoma	1 (2)
Stones GU tract	10 (19.6)
Other benign causes	31 (60.8)
36-months followup	
Urothelial carcinoma of bladder	1 (6.7)
Renal carcinoma	2 (13.3)
Stones GU tract	8 (53.3)
Prostate cancer	1 (6.7)
Other benign causes	3 (20)
Beyond 36 months' followup	
Urothelial carcinoma of bladder	2 (15.4)
Stones GU tract	4 (30.8)
Other benign causes	7 (53.8)

GU: genitourinary; MH: microscopic hematuria.

Table 3. Association of patient demographics and characteristics with GU cancer (all grades) and high-grade GU cancer

Variable	Reference	GU cancer (all grades)			High-grade GU cancer		
		OR	95% CI for OR min–max	p	OR	95% CI for OR min–max	p
Male	Female	2.958	1.922–4.666	<0.001*	3.012	1.964–4.735	<0.001*
Age years	Per unit increase	1.033	1.017–1.051	<0.001*	1.033	1.016–1.050	<0.001*
Prior GH (>12 months with negative workup)	No history of prior GH	3.469	2.101–5.607	<0.001*	4.195	2.592–6.66	<0.001*
Smoking status (high score)	Smoking status (low score)	1.048	0.682–1.582	0.824	1.069	0.698–1.610	0.752
High-grade MH >25 RBC/HPF	Low-grade MH ≤25 RBC/HPF	2.977	1.592–5.380	<0.001*	0.796	0.738–1.089	0.220
Prior LUTS	No prior LUTS	0.081	0.004–0.380	0.014*	0.088	0.005–0.405	0.016*
Family history of GU cancer	No family history of GU cancer	1.149	0.510–2.318	0.715	1.169	0.521–2.350	0.683
Prior abdominopelvic radiation	No prior abdominopelvic radiation	0.620	0.212–1.609	0.350	0.594	0.204–1.550	0.309
Prior chemotherapy	No prior chemotherapy	2.473	0.734–6.933	0.108	2.435	0.718–6.866	0.117
Chronic analgesic use	No chronic analgesic use	1.099	0.238–3.502	0.887	1.018	0.225–3.179	0.978
Distance to provider km	Per unit increase	0.999	0.997–1.000	0.227	0.998	0.994–1.000	0.173

*Statistically significant. CI: confidence interval; GH: gross hematuria; GU: genitourinary; HPF: high power field; LUTS: lower urinary tract symptoms; MH: microscopic hematuria; OR: odds ratio; RBC: red blood cell.

sis was 4.81% (95% CI 4.70–4.93%) at three months, 6.65% (95% CI 6.51–6.78) at one year, and 12.34% (95% CI 12.15–12.53) at five years.[29] These findings underscore the long-term malignancy risk following a hematuria diagnosis. Similarly, Hansen and colleagues reported a pooled PCa prevalence of 1.4% (95% CI 0.8–2.2, n=71/6642) among patients with MH, further highlighting the diagnostic relevance of this common urologic finding.[30]

A strong association was observed between MH, male sex, advanced age, and GU cancer risk, consistent with previous studies. In our cohort, male sex was independently associated with an almost threefold increased risk of GU cancer (OR 2.958, 95% CI 1.922–4.666, p<0.001). Patients with cancer were also significantly older than those without cancer (mean age 58.5±10.7 vs. 50.5±14.2 years, p<0.001). Large-scale studies, including a meta-analysis by Jeppson and colleagues[31] and a population-based study by Loo et al,[32] have demonstrated a higher predictive value of MH in men, with reported positive predictive values (PPV) ranging from 1–11%.

Jeppson et al's meta-analysis, which included eight of 17 studies conducted exclusively in women, showed that sex and age are key factors in the evaluation of MH.[31] The PPV for urothelial carcinoma increased from 2.1% to 6.2% in men aged ≥50 years, while the risk among women with MH was 2.01%. The authors estimated that 859 women (95% CI 654–1250) with MH would need full evaluation to detect one GU malignancy.[31]

Samson and colleagues studied 1049 patients with MH and found that male sex was significantly associated with GU malignancy (10 males vs. two females, p=0.005).[33] The median age of patients with malignancy was 68.7 years, compared to 57.3 years in those without (z=-3.644, p=0.0003).

Although females accounted for 56.7% of MH cases in our study, they had significantly lower GU malignancy rates. In the study by Loo et al, the overall rate of urologic cancer in women was 1.3% (47 of 3573).[32] Using a cutoff of 60 years, the cancer rate was 0.6% (13 of 2053) in women under 60, compared to 2.2% (34 of 1,520) in those ≥60 years (p<0.01). Additionally, a history of GH markedly increased the cancer detection rate from 0.8% (27/3227) to 5.8% (20/346) (p<0.01).[32] This sex-based disparity supports existing risk models prioritizing male sex as a stronger clinical factor and may justify more conservative evaluation in low-risk female patients.

In our study, a history of GH increased the odds of detecting cancer nearly threefold (OR 3.469, 95% CI 2.101–5.607, p<0.001). High-grade MH was slightly more common in the cancer group compared to the non-cancer group, reaching statistical significance

(p=0.029). When included in the regression model, high-grade MH remained significantly associated with GU malignancy (OR 2.977, 95% CI 1.592–5.380, p<0.001), although it was not associated with higher-grade tumors (p=0.220). Additionally, there is a 16.3% risk of cancer in patients presenting with MH who have a prior history of GH, strongly supporting the need for close followup in this specific group.

These findings are consistent with previous reports. In the study by Lippmann et al, a history of GH was associated with an OR of 6.2 (95% CI 3.4–11.5).[34] Similarly, Lisanti and colleagues reported that GH significantly increased cancer risk in both males (OR 2.35, p=0.001) and females (OR 4.25, p<0.001).[35] In contrast, Samson et al did not identify a significant correlation between RBC count and malignancy, underscoring that the diagnostic utility of hematuria grade may vary depending on the study population and clinical context.[33]

Despite its established association with GU malignancies in prior epidemiologic studies, smoking history was not significantly associated with cancer in our cohort (OR 1.048, p=0.824). This may be attributed to the unusually high baseline smoking prevalence in NWO, exceeding 30% in both cancer and non-cancer groups. Similar trends have been observed in other regional studies, where elevated population-level smoking rates appear to dilute its predictive value. While smoking has been implicated in GU cancer, Barbosa et al found no strong association between smoking intensity and bladder cancer aggressiveness.[36] This is consistent with findings by Ho and colleagues in the REDUCE trial, which showed that smoking was not associated with PCa diagnosis but was linked to an increased risk of higher-grade disease.[37]

In a meta-analysis by Al-Fayez et al, which included 15 studies, smoking was found to have an inverse association with PCa incidence, with a reported relative risk of 0.84 (95% CI 0.78–0.91).[38] In contrast, Samson et al reported a significantly higher cancer incidence in smokers compared to non-smokers (3.6% vs. 0.3%; 10 smokers vs. two non-smokers; p<0.0001).[33] Similarly, Lippmann et al found a significant association between smoking and GU cancer, with an OR of 3.2 (95% CI 1.8–5.9).[34]

Another notable finding in our study was the inverse association between LUTS and malignancy. LUTS appeared to offer a low probability of GU malignancy, with an OR of 0.081 (p=0.014). Recurrent UTIs were more prevalent among non-cancer patients, suggesting that these symptoms often point to benign etiologies.

Fankhauser et al similarly reported that most patients presenting with MH and LUTS were ultimately diagnosed with benign conditions.[39] Sarier et al also found that while the coexistence of LUTS and MH was common, its sensitivity for detecting cancer was low (21.7%, 95% CI 18.84–24.86).[40] These findings raise important questions about whether LUTS in the context of MH may reflect a lower likelihood of malignancy or simply suggest the need to investigate more common benign causes first, particularly in female patients.

Our study demonstrated that the likelihood of detecting a new malignancy following a negative initial workup was low, with a rate of approximately 1.4% over 36 months. This finding is supported by Lisanti et al, who reported a malignancy risk of less than 1% after an initial negative evaluation.[35] Similarly, Saxon et al identified only one malignancy during followup among more than 4456 women, in addition to 13 malignancies detected at initial presentation.[41] These findings raise the question of whether a more conservative followup strategy may be appropriate in select low-risk patients and whether prolonged surveillance is necessary in all cases, while recognizing that followup intensity may differ based on clinical judgment and local practice patterns.

While the proportion of incidentally detected tumors has risen to 48–66% in recent years, most are localized renal cancer tumors at presentation and are associated with favorable outcomes following surgical management. In Özsoy et al's study, the rate of incidental renal cell carcinoma discovered during PCa evaluation was 1%, suggesting that some cancers detected during followup may reflect the natural background incidence of incidentally identified renal lesions that were not detectable at the time of the initial MH workup.[42] These observations support the interpretation that the MH evaluation is primarily valuable for the prompt detection of urothelial carcinoma, whereas the detection of other primary GU malignancies more closely aligns with incidental findings reported in broader imaging literature.

In our study, the mean distance to healthcare providers did not differ significantly between cancer and non-cancer patients. While geographic barriers can influence access to care and contribute to diagnostic delays, our findings suggest that, despite the remote geography of the region, diagnostic pathways were relatively effective. Fletcher et al reported that individuals with Medicaid or no insurance were nearly twice as likely to experience delayed bladder cancer diagnosis compared to those with private insurance (uninsured OR: 1.90, 95% CI 1.70–2.12; Medicaid OR: 2.03, 95% CI: 1.87–2.20).[43] These patients also had higher bladder cancer-specific

mortality due to delayed intervention and lower odds of receiving treatment (uninsured adjusted hazard ratio [AHR]: 1.49, 95% CI 1.31–1.71; Medicaid AHR: 1.61, 95% CI 1.46–1.79).[43] These findings support the notion that barriers to healthcare access can negatively impact cancer detection, particularly in rural and Indigenous communities where healthcare inequities may be more pronounced.

In the context of rising healthcare costs and increasing awareness of the environmental impact of extensive diagnostic testing, our findings support a more conservative, risk-stratified approach to the evaluation of MH. Given the low rate of delayed high-risk malignancy and the high prevalence of benign etiologies on followup, a uniform, aggressive workup for all patients represents significant resource utilization (time, money, and materials). A risk-based strategy that prioritizes evaluation in patients with high-risk clinical features may help optimize resource allocation, reduce unnecessary investigations, and avoid over-evaluation of low-risk individuals.

Limitations

When interpreting our findings, a few important limitations should be considered. The retrospective design may introduce selection and information bias, and data accuracy was reliant on the completeness of EMRs. Additionally, despite a priori covariate selection, the number of events per variable may raise concern for potential model overfitting. The high prevalence of smoking and the regional healthcare context in NWO may affect the generalizability of our results to other settings. Furthermore, the followup period may not have been long enough to capture delayed cancer diagnoses, and diagnostic evaluations and imaging were not uniformly applied across all patients. Prospective, multicenter studies with standardized diagnostic protocols and longer followup are needed to confirm these findings and support improved risk stratification in patients with MH.

CONCLUSIONS

This study highlights the clinical relevance of male sex, age, prior GH, and high-grade MH (>25 RBC/HPF) as factors associated with urologic malignancy in NWO. With a 5.2% prevalence of GU cancer among patients with MH, our findings may support re-evaluating current guidelines to improve risk-stratification and diagnostic pathways. Prioritizing patients with high-risk features during followup may help optimize resource allocation and minimize overevaluation in low-risk individuals. Further studies in diverse settings are warranted to validate these findings and assess guideline adequacy for MH.

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