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# Assessment and Cost Analysis for Patients Admitted to Emergency Department with Macroscopic Hematuria

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## Abstract

**Aim:** This study examined the etiological causes and their cost analysis in patients admitted and hospitalized with macroscopic hematuria (MH).

**Materials and Methods:** Hemograms, urine, and biochemistry results of patients with MH, radiological images and pathology results, hospitalization need, hospitalization durations, and hematuria causes acquired following hospitalization, and the expenditures during this phase were registered for the patients. Laboratory values for the detected hematuria causes were compared and examined statistically.

**Results:** Seventy-eight patients admitted to the emergency department with MH were evaluated. The most common underlying pathologies were bladder cancer (34.6%, n=27), prostate pathologies (24.3%, n=19), kidney stone (8.9%, n=7), urethral stone (7.7%, n=6), kidney cancer (7.7%, n=6), bladder stone (6.4%, n=5), urinary infection (6.4%, n=5), kidney laceration (2.6%, n=2) and arteriovenous malformation (1.3%, n=1) respectively. The mean invoice amount covering the management starting from admission with MH was 6647±10200₺ for each patient. In operated patients (n=54), hospitalization duration, catheterization duration, and invoice amount were found to be higher; in patients with malignancy (n=34) age, hospitalization duration, catheterization duration, and invoice amount were higher ($p<0.05$, all parameters).

**Conclusion:** Among patients with MH, those with indications for surgery and malignancy have a greater impact on health expenditure. We can conclude that it will be beneficial for both the patient and the economy to start the diagnosis and treatment process before the onset of MH with prevention and early screening workups.

**Keywords:** Cancer, hematuria, malignancy, operation, urolithiasis

## Introduction

Macroscopic hematuria (MH) is the presence of blood visible through the naked eye in urine [>50 erythrocytes per high-power field (HPF)] (1). Even 1 mL of blood in a liter of urine causes visible hematuria (2). Benign or malignant masses, stone disease, infection, trauma, iatrogenic causes, vascular malformations, and nephrological diseases can be named among MH causes (2). MH is the isolated alarm symptom with the highest positive predictive value (PPV) for cancer (3). Studies detected no identifiable cause in 50% of macroscopic and 70% of microscopic hematuria patients (4).

The first approach for patients admitted with MH is examined under three headings; ensuring hemodynamic stability, detection of the underlying cause of hematuria, and ensuring urinary drainage (5).

Following confirmation of the diagnoses through further examinations in the urology clinic after hospitalization, treatment of the diagnosis can be started. Diagnostic methods such as intravenous pyelography, ultrasonography, computed tomography, cystoscopy, angiography, magnetic resonance imaging, and biopsy can be used for etiological investigations. The characteristics of underlying diseases are important for the clinician to avoid delaying certain diagnoses and effective treatments of the patients. The economic burden of MH is also worthy to be underlined since it is an alarming symptom of urological malignancies and stone disease (6).

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The aim of our study was to examine the etiological causes presented in patients admitted to our hospital and hospitalized following the detection of MH and to examine their cost analysis.

## Materials and Methods

The study is conducted as a retrospective cohort study after obtaining approval from the Necmettin Erbakan University Meram Faculty of Medicine of Local Ethics Committee (date: 07.10.2022, decision no: 2022/3992). The data of patients who had been admitted to a tertiary university hospital emergency department with first time MH complaint between January 2017 and January 2022 were analyzed retrospectively and the acquired data were registered and examined statistically. Blood visible in the urine through the naked eye and detection of more than 50 erythrocyte/HPF in urinalysis were MH.

Priorly studied hemograms, urine, and biochemistry results of patients with MH, radiological images, and pathology results, hospitalization need, hospitalization durations, and terminal diagnoses acquired following hospitalization in operated and non-operated patients; in malignancy-found and found patients; and the expenditures of the patients during this phase were registered, analyzed, compared, and examined statistically.

**Study Exclusion Criteria:** Iatrogenic hematuria causes (catheterization, operation history, etc.), patients with known hematuria-causing diseases, patients under the age of 18, and pregnant women were excluded from the study.

### Statistical Analysis

Power analysis was conducted with the acquired definitive measurements to determine the size of ideal sampling for the study. The effect size in the power analysis conducted according to catheterization and hospitalization definitive measurements was calculated as d=0.80. The sample size was calculated as 17 for catheterization and 22 for hospitalization for both groups when the error level was determined to be 5% and the power value 95%. The number of patient populations reached a minimum of twenty-four for each subgroup. The study was completed with this sampling because 78 patients were reached during the study period. Statistical analyzes of the data acquired in the research were performed using Statistical Package for Social Sciences 23.0 (Statistical Package for Social Sciences, Chicago, IL, USA) program. The presence of normal data distribution was tested through the One-Sample Kolmogorov-Smirnov test, and it was detected that the data had a normal distribution.

Categorical variables were shown as frequency and percentage, and constant variables were shown as mean±standard deviation. Chi-square analysis was used for categorical variables and independent T and Mann-Whitney U tests were used for the comparison of two groups for constant variables. Pearson correlation analysis was carried out to constant variables. $P<0.05$ was accepted as statistically significant in all assessments.

## Results

Seventy-eight patients admitted to the emergency department with MH were assessed. The demographic data of the study group are presented in Table 1. The most common comorbid diseases were diabetes mellitus (34%) and hypertension (25%), and 20% of the patients had no secondary disease. 70% of the patients were not on anticoagulant therapy. The most commonly used anticoagulant was acetylsalicylic acid with a percentage of 15.5%. The anticoagulant use and type of patients are presented in Table 1. All patients underwent radiological examination (Table 1). Clot retention was detected in 27 patients (34.6%). The most common underlying pathology was bladder cancer (34.6%, n=27) (Table 1). Urological malignancy was detected in 43.5% of the patients (n=34). These malignancies were detected as bladder cancer in 34.6% (n=27), upper urinary system collective cancer in 5.1% (n=4), renal cancer in 2.6% (n=2), and prostate cancer in 1.3% (n=1). The following admission with hematuria, 54 patients (69.2%) were operated in the urology department. Mean values for MH patients were 7.1±5.5 days for hospitalization and 6.4±5.2 days for catheterization. The mean invoice amount covering the management starting from admission with MH was measured as 6647±10200₺ for each patient. General information for the patients is provided in Table 1.

Based on laboratory values, hemoglobin level was below the lower limit (11.4 gr/dL) and creatinine, blood leukocyte, and C-reactive protein (CRP) levels were high. Laboratory values of hematuria patients are provided in Table 2.

In subgroup analysis, operated (n=54) and non-operated (n=24) patients were compared to patients with (n=34) and without (n=44) malignancy as the underlying pathology.

As expected, a significant difference was detected only between hospitalization duration, catheterization duration, and invoice amount among operated and non-operated patients. These parameters were significantly high in operated patients ($p<0.05$ for all parameters). Significant parameters for operated and non-operated patients are presented in Table 3 and Figure 1 in detail.

A significant difference in age, hemoglobin, hospitalization duration, catheterization duration, and invoice amount was detected among patients with (n=34) and without (n=44)

| Table 1. General information for macroscopic hematuria patients | |
|---|---|
| **Age (years)** | 69.6±17.1 |
| **Gender n (%)** | |
| Male | 67 (85.9) |
| Female | 11 (14.1) |
| **Oral anticoagulant/antiplatelet n (%)** | 23 (29.5) |
| ASA | 12 (15.5) |
| DOAC | 5 (6.4) |
| LMWH | 3 (3.8) |
| Warfarin | 3 (3.8) |
| **Radiological examination n (%)** | |
| US | 24 (30.8) |
| CT and/or MRI | 54 (69.2) |
| **The underlying etiological factor n (%)** | |
| Bladder cancer | 27 (34.6) |
| Prostate pathologies | 19 (24.3) |
| Prostate cancer | 1 (1.3) |
| Benign prostate causes | 18 (23) |
| Kidney stone | 7 (8.9) |
| Ureteral stone | 6 (7.7) |
| Kidney cancer | 6 (7.7) |
| Renal cancer | 2 (2.6) |
| Urinary system collective cancer | 4 (5.1) |
| Bladder stone | 5 (6.4) |
| Urinary tract infection | 5 (6.4) |
| Renal laceration | 2 (2.6) |
| AVM | 1 (1.3) |
| **Surgery indication n(%)** | 54 (69.2) |
| **Catheterization duration (day)** | 6.4±5.2 |
| **Hospitalization duration (day)** | 7.1±5.5 |
| **Invoice amount (₺)** | 6647±10200 |

ASA: Acetylsalicylic-acid, DOAC: Direct acting oral anticoagulants, LMWH: Low molecular weight heparin, US: Ultrasound, CT: Computed tomography, MRI: Magnetic resonance imaging, AVM: Arteriovenous malformation

| Table 2. Laboratory values for macroscopic hematuria patients | |
|---|---|
| **Parameters** | |
| **Hemoglobin gr/dL** | 11.4±2.36 |
| **Platelet ($10^3$)/mm$^3$** | 244±109.8 |
| **WBC ($10^3$)/mm$^3$** | 12.03±9.2 |
| **Urea mg/dL** | 51.4±34.3 |
| **Creatinine mg/dL** | 1.36±0.86 |
| **CRP mg/L** | 35.6±54 |
| **aPTT s** | 28.3±5.7 |
| **PT s** | 15.3±12 |
| **INR** | 1.16±0.48 |
| **AST u/L** | 22.9±21.2 |
| **ALT u/L** | 19.8±22.9 |
| **Urine Ph** | 5.6±0.4 |
| **Urine erythrocyte (+)** | 2.84±0.5 |
| **Urine leukocyte (+)** | 0.9±1 |

WBC: White blood cell, CRP: C-reactive protein, aPTT: Activated partial thromboplastin clotting time, PT: Prothrombin time, INR: International normalised ratio, AST: Aspartate aminotranferase, ALT: Alanine aminotransferase

malignancy as the underlying MH cause. In patients with malignancy, hemoglobin was found to be lower while age, hospitalization duration, catheterization duration, and invoice amount were found higher ($p<0.05$ for all parameters). Significant parameters for patients with and without malignancy are presented in Table 4 and Figure 2 in detail.

The correlation analysis detected a negative correlation between hemoglobin level and age ($r=-0.35$, $p=0.02$), creatinine level ($r=-0.24$, $p=0.03$) and invoice amount ($r=-0.22$, $p=0.04$) (Figure 3, Table 5).

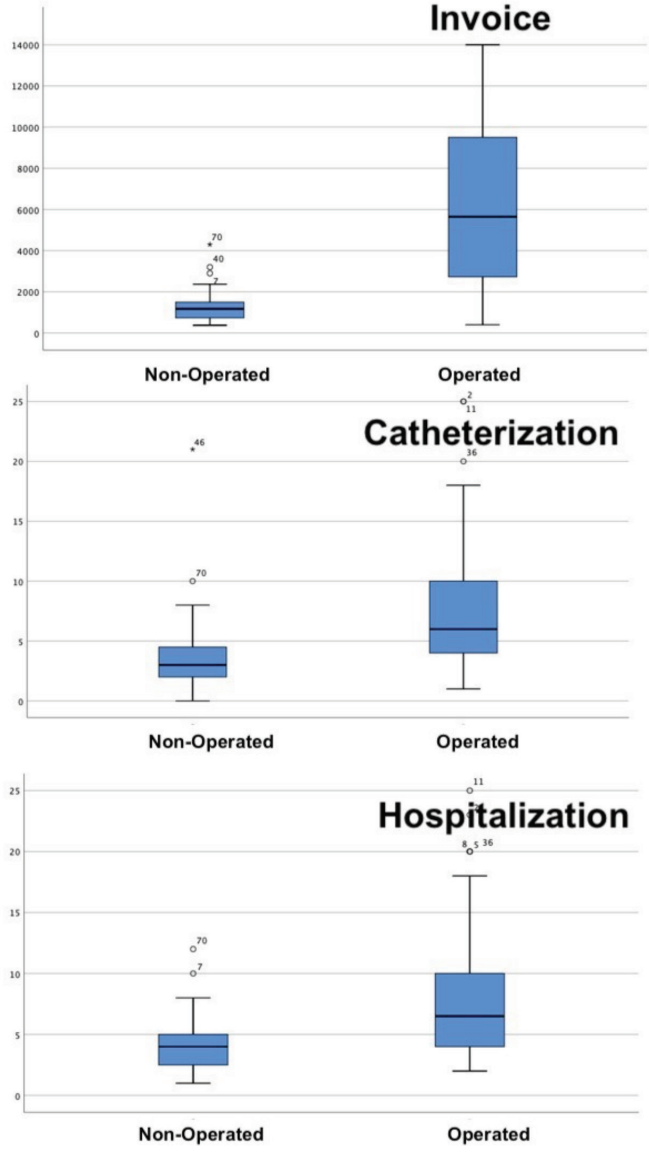


**Figure 1.** Graphic for significant parameters between operated and non-operated patients

## Discussion

MH is among emergency department admission causes and may be presented as a symptom of various underlying diseases. One of these diseases is urological cancers (6), which were detected in 66% of the patients with MH (7); in our study, this rate was found 43.6%. Bladder cancers constitute most malignancies detected in patients admitted with MH (n=255/317, 80%) (7) and are the ninth most prevalent cancer type and the thirteenth most common cause of cancer-related deaths globally (8). Microscopic or MH in urine constitutes the most common symptoms of bladder cancer with rates of 13.7% and 78.3%, respectively. The PPV of MH was reported as 0.83 in bladder cancer (95% CI=0.80-0.85), 0.66 in urethral cancer (95% CI=0.53-0.77), 0.48 in renal cancer (95%) CI=0.36-0.60) and 0.22 (0.17-0.27) for all urological cancers (7). In another study, the PPV of MH in urological cancers was reported as 10.3% (95% CI=7.6% to 13.7%) and its sensitivity was reported as 59.5% (95% CI=50.4% to 60.1%). In a study regarding gender, the PPV was reported as 22.1% (95% CI=15.8% to 30.1%) in males and 8.3% (95% CI=3.4% to 17.9%) in females among all patients over the age of 60. Urological cancer was not detected in the patient group under the age of 40 in the prospective part of the study (9). Another study assessed 1697 patients in which 83% of these were reported as bladder cancer, 6% as renal cell carcinoma, 5% as prostate cancer, 2% as ureteric urothelial carcinoma, 2% as gynecological cancer, 2% as renal pelvis urothelial carcinoma,

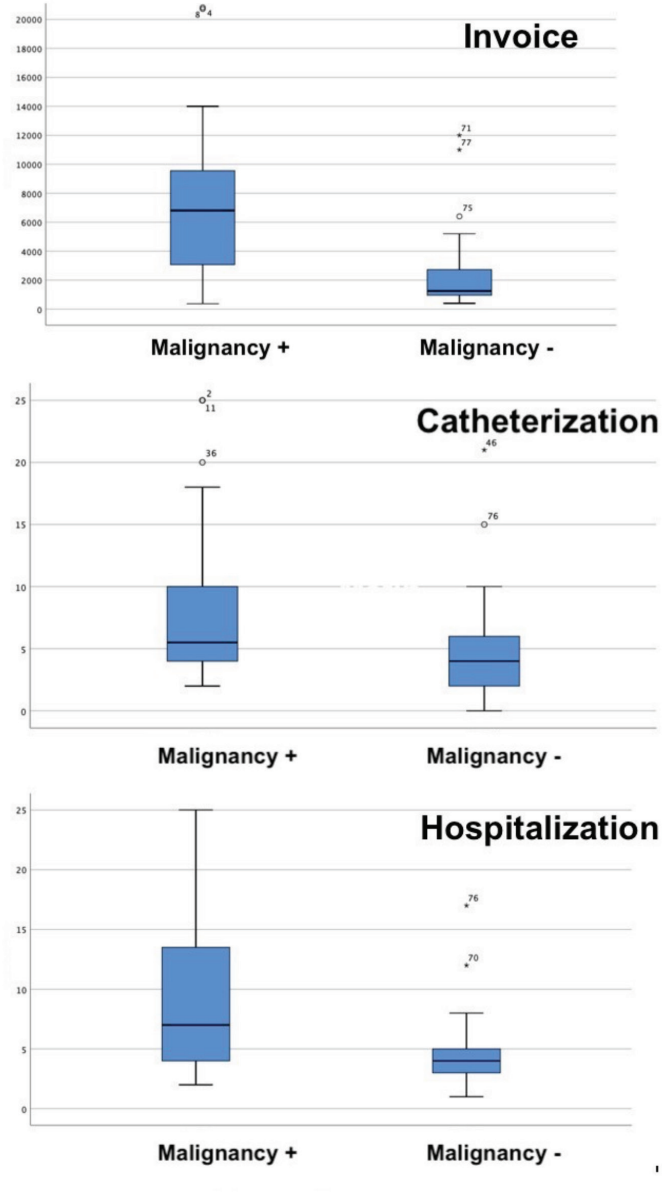


**Figure 2.** Graphic for significant parameters between patients with and without malignancy patients

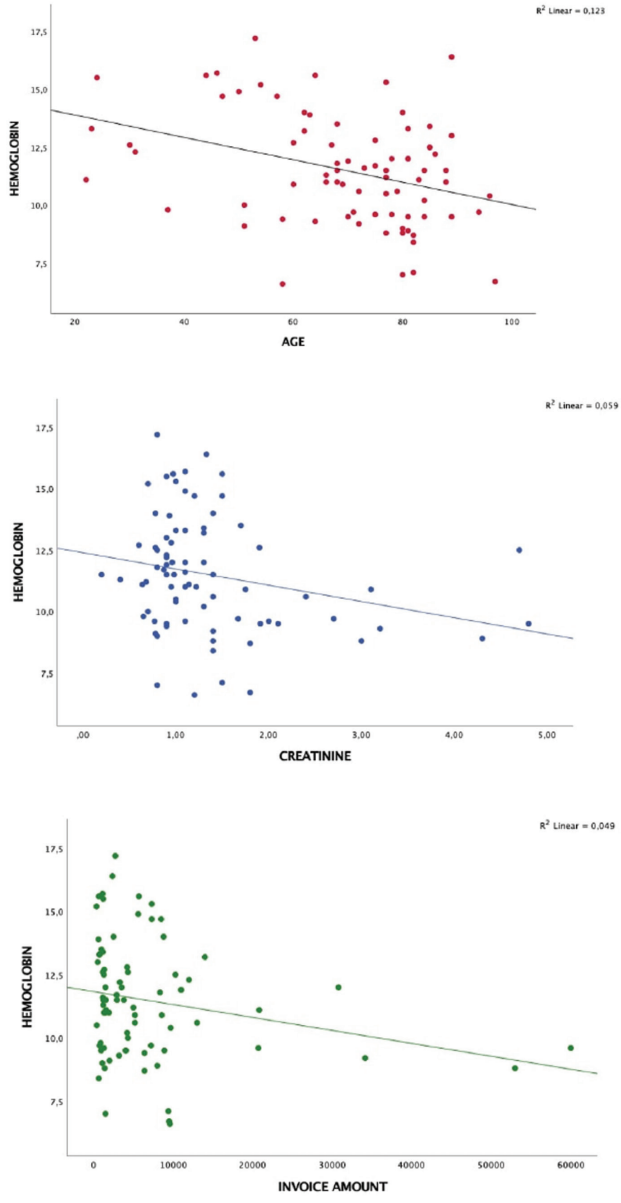


**Figure 3.** Graphic for significant parameters of correlation analysis

| Table 3. Significant parameters between operated and non-operated patients | | | |
|---|---|---|---|
| | **Operated n=54** | **Non-operated n=24** | **p** |
| **Catheterization duration (day)** | 7.4±5.4 | 3.2±2.5 | **0.001** |
| **Hospitalization duration (day)** | 8.3±6 | 4.2±4.1 | **<0.001** |
| **Invoice amount (₺)** | 8981±11587 | 1395±949 | **<0.001** |

| Table 4. Significant parameters between patients diagnosed with and without malignity | | | |
|---|---|---|---|
| | **Malignancy (+) n=34** | **Malignancy (-) n=44** | **p** |
| **Age (year)** | 73.77±11.9 | 64.2±21.1 | **0.01** |
| **Hemoglobin gr/dL** | 10.9±2.3 | 12.1±2.1 | **0.02** |
| **Catheterization duration (day)** | 7.7±5.7 | 4.4±4.1 | **0.001** |
| **Hospitalization duration (day)** | 8.9±6.4 | 4.8±3 | **<0.001** |
| **Invoice amount (₺)** | 10000±12689 | 2483±2756 | <0.001 |

| Table 5. Details of correlation analysis | | | | | | |
|---|---|---|---|---|---|---|
| **Parameters** | **Age** | | **Creatinine** | | **Invoice amount** | |
| **Hemoglobin** | **R** | **p** | **r** | **p** | **r** | **p** |
| | -0.35 | 0.02 | -0.24 | 0.03 | -0.22 | 0.04 |

and 1% as other cancers (10). The cost per patient is higher in bladder cancer compared with other cancer types based on the recurrence prevalence, progression possibility, and lifelong follow-up requirement (11). In a study conducted in Japan, where there is a national mass screening program, Specific Health Checkup, since 2008 and all adults between 40 and 74 years of age are targeted, dipstick urine tests for proteinuria and glucosuria are part of the SHC, however, dipstick urine tests for hematuria are not. So Okubo et al. (12) made a research on the hematuria test's cost-effectiveness and concluded that mandating the dipstick hematuria test could be cost-saving. In line with the literature, the most common MH causes in our study were bladder cancer [34.6%, (n=27)], and upper urinary system collective cancer with 5.1% (n=4), renal cancer with 2.5% (n=2), and prostate cancer with 1.3% (n=1) followed it, respectively. Patients with (n=34) and without (n=44) malignancy as the underlying pathology were compared in the subgroup analysis performed, and a significant difference between age, hemoglobin, hospitalization duration, catheterization duration, and invoice amount was detected among these patients. Hemoglobin was found to be lower, whereas age, hospitalization duration, catheterization duration, and invoice amount were found to be higher in patients with malignancy ($p<0.05$ for all parameters). Significant parameters for patients with and without malignancy are presented in Table 4 and Figure 2 in detail.

Passing kidney stone and thus renal colic constitute the ninth most common emergency department admission cause (13), and urinary tract stone is the most common MH cause in patients under the age of 40 (14). In a study investigating 50 patients admitted to the hospital with MH, urolithiasis was found as the etiological cause in 22% (15). MH was reported in 30% of the patients diagnosed with urolithiasis (16). The study of Nilbert et al. (10) assessed 1697 patients due to MH, benign causes were detected in 1034 patients, and 13% (n=136) of these benign causes were reported as upper urinary system stones and 3% (n=33) as bladder stones; these rates were 8% and 1%, respectively, when calculated according to total gross hematuria patients. The 3rd and 4th most common MH causes were detected as kidney stone (8.9%, n=7) and urethral stone (7.7%, n=6) in our study. Bladder stone was 6th most common with a rate of 6.4% (n=5). Lower rates in our study compared with similar studies may be due to the inclusion of only hospitalized MH patients in the study. Most kidney-stone-related costs are caused by emergency department visits and inpatient treatment. When appropriate, patient management through outpatient treatment and stone prevention strategies will be related to potentially lower costs. An analysis using national data reported that stone disease costed 2.1 billion dollars in 2000 and this amount covered hospitalization expenses of 971 million, specialist inspection and outpatient treatment of 607 million, and emergency department admissions of 490 million (17). Annual health expenditure was reported as 3038 dollars in patients without and 6532 dollars in patients with kidney stones, and the presence of stone disease was observed to cause a cost increase of nearly two times (18). The invoice amount was 2483±2756₺ in our study in malignancy-

negative patients, and this amount also covered urolithiasis patients. Detection of a significantly shorter hospitalization duration in malignancy-negative patients in our study is among the cost-lowering factors.

A review reported that urinary tract infection constitutes 33% of the underlying causes in 1200 MH patients (19). In Nilbert et al.'s (10) study on 1697 patients with MH, benign causes were detected in 1034 patients, and 45% of these benign causes (n=649) were related to urinary tract infection. In another study evaluating 275 patients with MH who were contacted through "red phone", the urinary tract infection rate was detected 10% (n=28) (20). The annual cost of community-acquired urinary tract infection is approximately 1.6 billion dollars in the United States (21). With a higher rate, especially in women, it was previously reported that urinary tract infection may delay bladder cancer diagnosis and thus patients who were admitted with MH and were detected to have urinary tract infection could have concurrent bladder cancer (22). Hence, it is also possible that the urinary tract infection may cause a delay in diagnosis through masking bladder cancer and increasing the cost.

Among total MH causes, urinary tract infection was detected as 6.4% (n=5) in our study, and with a prevalence of 11% (n=5) among benign causes (n=44), it was detected as the third most common benign cause after stone diseases and benign prostatic causes and this finding was in line with the literature. However, its lower rate compared to other studies might be due to the fact that the underlying urinary malignancy was registered as the main diagnosis, although it was concurrent with urinary tract infection or early start of antibiotic treatment in primary care or emergency departments with the presence of high CRP.

Renal traumas constitute 1-5% of all traumas and 10% of abdominal traumas. Renal trauma must be suspected in cases of hematuria, but hematuria is not 100% sensitive or specific for renal trauma (23). A study assessing patients with kidney damage due to stab wounds did not detect hematuria in 9% of the patients (24). Kidney laceration was detected in 2.6% (n=2) of patients admitted with hematuria in our study. Among 14.590 patients hospitalized due to renal trauma in the United States, the mean trauma-related nephrectomy prevalence was reported as 5.3%, median hospitalization duration was 5 days, and median hospital cost was 28.975 dollars (25). Since the patients who had renal laceration in our study were grade 2-3, they had followed up without surgery. Thus, among malignancy-negative patients, cost analysis was found as 2483±2756₺, and hospitalization duration was 4.8±3; and among non-operated patients, cost analysis was found as 1395±949₺, and hospitalization duration was 4.2±4.1.

Renal arteriovenous malformations (AVMs) are rare benign lesions with an approximate rate of 0.04% (26). These are focal failures emerging during the formation of vascular structures in the 4-10$^{th}$ weeks of gestation and generally cause symptoms at the ages of 30-40 (27). Hematuria is the primary symptom in three out of every four AVM patients (28). In line with the literature, renal AVM was detected as a gross hematuria cause in 1.3% (n=1) of the patients in our study.

Cancer possibility was not found to be different from other patients in patients using anticoagulants among drugs modifying coagulation, non-steroidal anti-inflammatory drugs, and aspirin; thus, it was reported that the decision to assess hematuria patients should not be taken based on anticoagulant use (10). In our study, 29.5% of the patients were using coagulation inhibitors, and advanced was examined in all patients as described in the literature. To sum up, catheterization and hospitalization durations, the costs of patients who underwent surgery and had malignancy were found to be significantly high in our study. Among MH patients, those with surgical indications and malignancies have a higher influence on health expenditures. These findings show that starting the diagnosis and treatment process after the formation of MH has high costs. Therefore, we may conclude that reducing the expenditures through prevention such as cessation of smoking, secondhand smoke, tobacco use and chemical and environmental exposures; diet, physical activity, weight and sleep changes; and early detection methods such as simple urinalysis will be beneficial for the patient. Hence, the attitude and experience of emergency medicine physicians play a critical role in quick management, ensuring urine drainage, maintaining hemodynamic stability, application of appropriate radiological examinations, application and management of appropriate consultations, or providing accurate guidance.

### Study Limitations

Small number of patients, cost analysis only covering diagnosis and treatment costs within the hospital in a single admission, and the lack of evaluation of indirect causes (effect of lost time of travel, time- off work, loss of productivity, etc.) were the limitations of our study. Additionally, since our country does not have a national cancer screening or check-up program, mass screening costs compared to individual disease costs may vary.

## Conclusion

This study detected many etiological factors that could cause MH. The treatment process, prognosis, surgery requirement, and cost analysis of the patients differ based on etiological factors. Thus, the attitude and experience of emergency medicine physicians are important for quick management, ensuring urine

drainages, maintaining hemodynamic stability, application of appropriate radiological examinations, and the application and management of appropriate consultations. Catheterization and hospitalization durations and the costs of patients who were operated on and were found to be significantly high in our study. Among MH patients, those with surgical indications and malignancies have a higher influence on health expenditures. These findings show that starting the diagnosis and treatment process before the formation of MH through prevention and early detection methods will be beneficial for the patient and economy. Additionally, obtaining appropriate management in the emergency departments where the first admission point is plays a critical role in this.

### Ethics

**Ethics Committee Approval:** The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki. The study was approved by the Necmettin Erbakan University Meram Faculty of Medicine of Local Ethics Committee (date: 07.10.2022, decision no: 2022/3992).

**Informed Consent:** Retrospective study.

**Peer-review:** Externally and internally peer reviewed.

### Authorship Contributions

Surgical and Medical Practices: M.K.A., A.A., Concept: L.Ö.S., M.K.A., A.A., Design: L.Ö.S., A.A., Data Collection or Processing: L.Ö.S., N.T., M.K.A., A.A., Analysis or Interpretation: L.Ö.S., A.A., Literature Search: L.Ö.S., M.K.A., E.E.Ö., A.A., Writing: L.Ö.S., N.T., M.K.A., E.E.Ö., A.A.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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