

# Prevalence and Management of Outpatients with Asymptomatic Microscopic Hematuria in a University Hospital

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**Background:** There has never been any report regarding the prevalence of asymptomatic microscopic hematuria (AMH) in the patients in the Southern part of Thailand. Additionally, there is also no data regarding clinical management for this kind of health condition.

**Objective:** To document the prevalence and management of AMH in outpatient departments of the region.

**Materials and Methods:** A cross-sectional descriptive study was conducted to analyze the clinical data of 511 patients, attending 10 outpatient departments of the hospital between January 2012 and May 2020. AMH was defined, according to the American Urology Association (AUA), as urine red blood cells in urine specimens greater than three per high power field, with no associated urinary symptoms.

**Results:** Among the 511 studied samples recruited for analysis, 73.0% of the AMH identified patients were female. The most common age and gender group was 56 to 65 years at 9.0% in males and at 24.7% in females, or about one-third of all age and gender groups. The patients from four departments, which usually send routine patient urinary examinations, including, General practice, the Primary care unit, Premium checkup, and Health care personnel surveillance, constituted of more than one-half at 56.4%, of all AMH patients from all departments. The most common investigation was repeated urinary analysis at 445/484 (91.9%), followed by urinary system imaging at 375/484 (77.5%). The most common management combination was repeated urine analysis and urinary system imaging, with urologist consultation at 225/484 (46.5%).

**Conclusion:** AMH is a common health condition in outpatient settings, and the patients were well managed for further investigation, according to AUA guidelines.

**Keywords:** Asymptomatic; Microscopic, Hematuria, Prevalence, Management, Investigation, Red blood cell

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Hematuria is a health condition characterized by the presence of red blood cells (RBCs) in the urine. Hematuria can be classified by the abundance of RBCs into gross hematuria and microscopic hematuria. Gross hematuria is defined as blood in the urine that is visible by the naked eye. The definition of microscopic hematuria is defined by the American Urological Association (AUA) as the presence of three or more RBCs per high power field<sup>(1)</sup>. Microscopic

hematuria can be asymptomatic or symptomatic, about the symptoms related to urinary system manifestations.

The initial investigation in cases of asymptomatic microscopic hematuria (AMH) should require calculated estimated glomerular filtration rate (eGFR), serum creatinine, and blood urea nitrogen (BUN). The presence of proteinuria, RBC cast, dysmorphic RBCs in the urine or any other symptom compatible with renal disease should be referred to a nephrologist. For the urologic evaluation of AMH, cystoscopy should be performed on all patients aged over 35 years, who present with risk factors for urinary tract malignancies. The initial evaluation for AMH should include a radiologic evaluation and multi-phasic computed tomography urography (CTU), including sufficient phases, to evaluate the renal parenchyma to rule out a renal mass in addition to an excretory phase to evaluate the urothelium of the upper urinary tracts. If a patient with a history of persistent AMH had two consecutive negative yearly urinalyses, no

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further urinalyses for evaluation of AMH is required. If a patient had persistent microscopic hematuria with yearly urine analysis (UA) earlier, re-evaluation and referral to nephrologists is recommended.

AMH is often under-recognized, and incidentally discovered by routine physical screening tests. The prevalence of AMH then varies widely among the reports from different countries and regions<sup>(2-5)</sup>. There are several guidelines recommended for the workup with AMH<sup>(4,6,7)</sup>. However, the evidence supporting the existing guidelines is mainly limited to expert opinion. In addition to the wide variation of potential causes associated with AMH, ranging from transient to malignancy<sup>(1,8,9)</sup>, the physician who identifies AMH is encountered with the decision of whether further investigation is required. If further investigation had to be conducted, the options of diagnostic protocols have broad clinical and economic implications, leading to diversities within medical practices.

The primary intention of the present study was to document the prevalence of AMH in the outpatient departments of a university hospital in the southern region of Thailand. In addition, the authors wanted to document the compliance of further investigations of patients with AMH compared with the recommendations of the AUA 2012 guidelines.

## Materials and Methods

### Setting

The present study was conducted in ten outpatient departments of Songklanagarind Hospital. The hospital belongs to the Faculty of Medicine, Prince of Songkla University. It is a medical school, with postgraduate training, and a referral center in Southern Thailand.

### Study design

A cross-sectional descriptive study was conducted to analyze the clinical digital data of patients attending the hospital between January 2012 and May 2020. The data were derived from the microscopic laboratory and the hospital clinical database information system.

### Participants

Adult patients, aged over 35 years old, with AMH identified by automat UA in the clinical microscopic laboratory unit were included. Since the data were retrieved from the patient's medical records and laboratory results, patient's informed consent could be exempted. The study protocol was approved by the Ethics Committee of the Faculty of Medicine, Prince of Songkla University (REC 63-428-9-4).

### Sample size

The sample size of 457 participants was based on  $P=0.05^{(10)}$ , including a 10% drop out. Therefore, the calculated sample size of the study were 500 participants.

### Inclusion criteria

Participants aged over 35, with RBCs in their urine specimen being greater than three per high power field and with no associated urinary symptoms were included.

### Exclusion criteria

Participants with conditions noted as gross hematuria, renal disease, infection, recent hospitalization, undergoing chemotherapy radiation, or malignancy as well as loss to follow up were excluded from the present study.

### Data analysis

The data were processed and consolidated using Microsoft Excel® spread sheet software. The patient's demographic data and physician management of AMH were summarized and reported as percentage. The confidence intervals of the percentage were calculated based on exact binomial statistics, using BINOM.INV function of Microsoft Excel®. The physician's choice of outpatient clinician care for AMH were also displayed in the Venn diagram. The trends of AMH managements were illustrated with a line graph.

## Results

After applying the exclusion criteria, the authors recruited 511 studied samples for analysis from 2,559 patients with microscopic hematuria. The demographic data and the department where the patients attended are displayed in Table 1. Almost three-fourths of the AMH patients were female (73.0%, 95% CI 69.1 to 76.7). The most common age-gender group was 56 to 65 with 9.0% in males (95% CI 6.7 to 11.5) and 24.7% in females (95% CI 20.9 to 28.4), or about one-third of all age-gender groups. Patients from four departments, which usually send routine urinary examinations, including General practice, Primary care unit, Premium checkup, and Health care personnel surveillance, constituted of more than one-half (56.4%) of all AMH patients from all departments.

Among the 511 patients included in the analysis, 25 patients received no further investigation nor consultation for the hematuria identified. The

**Table 1.** Demographic data and outpatient department attendance of 511 patients

Variable	n (%)	95% CI
Sex		
Female	373 (73.0)	69.1 to 76.7
Male	138 (27.0)	23.3 to 30.9
Male age group		
35 to 45	19 (3.7)	2.2 to 5.5
46 to 55	33 (6.5)	4.5 to 8.6
56 to 65	46 (9.0)	6.7 to 11.5
>65	40 (7.8)	5.7 to 10.2
Female age group		
35 to 45	60 (11.7)	9.0 to 14.7
46 to 55	113 (22.1)	18.6 to 25.8
56 to 65	126 (24.7)	20.9 to 28.4
>65	74 (14.5)	11.5 to 17.6
Outpatient department		
General practice	214 (41.9)	37.6 to 46.2
Medicine	143 (28.0)	24.1 to 31.9
Surgery	54 (10.6)	8.0 to 13.3
Primary care unit	50 (9.8)	7.2 to 12.5
Premium check up	18 (3.5)	2.0 to 5.3
Emergency room	11 (2.2)	1.0 to 3.5
Obstetrics and Gynecology	9 (1.8)	0.8 to 2.9
Healthcare personnel surveillance	6 (1.2)	0.4 to 2.2
Orthopedics	5 (1.0)	0.2 to 2.0
Ophthalmology	1 (0.2)	0.0 to 0.6
Total	511 (100)	

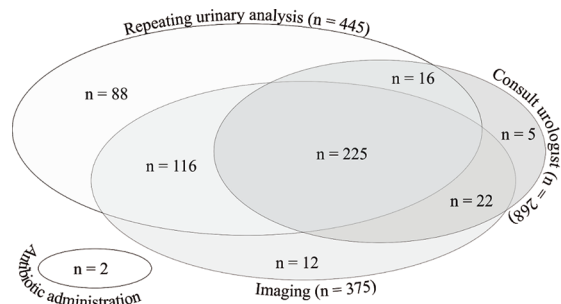
CI=confidence interval

remaining 486 patients were managed in overlapping and diversity of processes as illustrated using the Venn diagram in Figure 1.

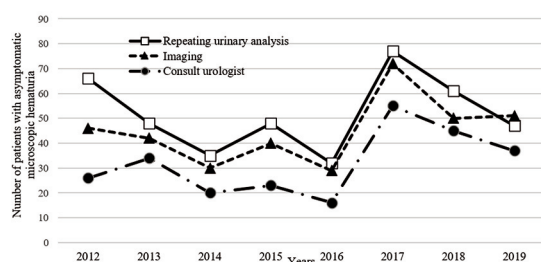
A Venn diagram is an illustration that uses circles to show the overlapping sets of data. In Figure 1, the most common investigation was repeated urinary analysis with 445/484 (91.9%), followed by urinary system imaging with 375/484 (77.5%). The most common management combination was repeated urine analysis and urinary system imaging, with urologist consultation with 225/484 (46.5%). The trends of AMH management after a patient was identified as AMH are illustrated in Figure 2.

## Discussion

An observational retrospective descriptive study, by retrieving and analyzing data from medical records, is a rapid way to identify clinical management in medical schools, where the data are extensively recorded. Therefore, the present research methodology was used as the primary study tool to



**Figure 1.** Venn diagram representing the sets of physician management for the 486 patients with asymptomatic microscopic hematuria (excluded 25 patients having no further management).



**Figure 2.** The prevalent trend of 511 patients with asymptomatic microscopic hematuria in outpatient department departments, categorized by management after identification.

evaluate whether further study in the authors hospital, in concerns to the underlying etiology of AMH, is feasible.

The present study was limited to patients over 35 years of age, because the AUA guidelines recommend prompt, further investigation of AMH at the age threshold of more than 35. The AMH in children is very rare and is most often spontaneously resolved<sup>(11,12)</sup>. Additionally, the study was dated back to the year 2012, to be compared with the AUA guidelines of 2012<sup>(12)</sup>.

The results of the present study show that the highest prevalence of AMH in both gender groups was in the age group of 56 to 65 years. The high prevalence in this male age group, compared to the other male age groups, may be explained by the high urinary malignancy in this age-gender group<sup>(13)</sup>. Additionally, the high prevalence in this female age group may be explained by more frequent contamination occurring from abnormal vaginal bleeding<sup>(14)</sup>.

The present study found the highest prevalence of AMH in female patients consistent with other studies<sup>(9,15,16)</sup>. However, the highest prevalence was found in the age group of 56 to 65 years. The results

of the present study also showed a very high number of patients being diagnosed with AMH. This indicates a common health condition in clinical practice<sup>(5,12,17)</sup>. Most of these (484/511, 94.7%), were investigated or referred to a specialist for underlying causes. The investigations were performed in different ways, and with different combinations (Figure 1). The management of AMH compiled very well with the AUA guidelines that recommends repeated urine analysis after identification of AMH. Repeated urine analysis was the most common investigation at 91.9%, with approximately one-half of patients being completely investigated by the three methods, for any underlying disease.

The prevalence of AMH as well as causes of AMH within this Southern region may differ from other areas. Apart from other causes, local vegetable consumption may play an important role in AMH, such as the djenkol bean (*Archidendron jiringa* or *A. lobatum*)<sup>(18)</sup>, which is a local, common bean consumed by people in the South. The djenkol bean contains djenkolic acid that may precipitate as needle-like crystals and causes hematuria in the population of this area<sup>(19)</sup>.

The strength of the present research includes updated physicians' management in outpatients with AMH in Songklanagarind Hospital and the AUA guideline management 2012.

There were limitations in the present study that warrant caution in interpreting the results. First, only tertiary-care hospital patients participated in the study. Consequently, the results, theoretically, may not be fully compatible for other populations receiving care in different facilities. Second, the methodological is attributed to retrospective chart reviews, wherein, repeated urinary analysis, imaging, and antibiotic administration were not regularly performed for all AMH cases in some outpatient departments of Songklanagarind Hospital. Third, the AUA guidelines were created for Urologist management, however, the authors used them for general practitioners and family physicians.

Further studies should be conducted to identify the underlying causes of AMH along with the predictors of each cause.

## Conclusion

The authors conclude from the present findings, that AMH is a common health condition in the outpatient settings, and that the patients were well managed concerning further investigation, according to the AUA guidelines.

## What is already known on this topic?

The prevalence of AMH varies widely among the reports from different countries and regions. There are several guidelines recommended for the workup of AMH. The physician who identifies AMH is encountered with the decision of whether further investigation is required, consequently, leading to diversities of medical practices.

## What this study adds?

This study found the highest prevalence of AMH was in female patients. Patients with AMH were well managed for further investigation, according to the AUA guidelines.

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## Conflicts of interest

All authors named in the present article certify that there are neither, financial nor non-financial conflicts of interest. All authors had full access to all of the data in this study and take complete responsibility for the integrity of the data as well as accuracy of the data analyses. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship of this manuscript, take responsibility for the integrity of the work, and have given final approval for this version to be published. All authors contributed to the study design, data collection and analysis, interpretation of results as well as to the writing and final approval of this manuscript.

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