

Overview of Erythrocyturia Pattern Among Eastern Sudanese Patients: A Study of the Diagnostic Pathway

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Abstract

Background: Hematuria is a prevalent finding encountered during manual routine urine examination in the laboratory. Two principle characters can be watched, microscopic and macroscopic hematuria. It tends to be clear for genuine urological conditions. Dysmorphic red blood cells (dRBCs) in urine deposit may be a successful incentive in the diagnosis of the glomerular and non-glomerular origin of hematuria. A cross-sectional observational study was enlisted to assess the capacity of dRBCs to perceive glomerular inception from another kidney hindrance. **Methods:** We have appraised 170 consecutive patients with hematuria at Dr. Awaad Medical Center, Red Sea State, Sudan from June 2017 to July 2018. Renal ultrasonography and urinalysis were performed. The statistical statements were analyzed using SPSS version 24.0 for windows. **Results:** Roughly 10/170 (5.9%) had gross hematuria, 49/170 (28.8%) had microscopic hematuria with clinical symptoms, 56/170 (32.9%) had microscopic hematuria with proteinuria, and 55/170 (32.4%) had isolated hematuria. The causes of hematuria were highlighted as (72.9% non-glomerular and 19.5% glomerular). dRBCs were encountered in 122/170 (71.8%) ($P = 0.000$) of an entire group of patients with hematuria. fRBCs were also detected in 99/170 (58.2%) of patients ($P = 0.000$) of an entire group of patients with hematuria. Of 170 patients, 50 (29.4%) had > 16.6 dRBCs and 47 (27.6%) had ≥ 12.0 fRBCs. dRBCs was sensitive (66.7%), specific (68.8%), with a positive predictive value (90.2%) for glomerular disease. Hematuria outcomes expressed as urinary tract infection (UTI) in (37.6%), followed by glomerulonephritis (19.5%), cystitis (18.2%), pyelonephritis (10.0%), and renal stones (7.6%). **Conclusion:** Urinary dRBCs > 16.6 in Urine sediment test was an extensive prognostic for glomerular illness, however, in joined with proteinuria it is explicit characteristic of the glomerular starting point. fRBCs were revealed to the non-glomerular origin. Dysmorphic RBCs persist in healthy subjects denotes a glomerular source. UTI, glomerulonephritis, and cystitis were considered the prevalent outcomes of hematuria in this report.

Keyword

Hematuria, dRBCs, Glomerular Disease, Albuminuria, Port Sudan

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1. Introduction

Hematuria spoke to about 6% of newfound anomalies recognized by urologists in routine laboratories. It had been evaluated as 4/1000 patients/year, by chance and can be available anyplace along with the urinary tract framework.

Notwithstanding, it could be seen as the first existed sign in genuine anomalies [1]. Asymptomatic hematuria might be characterized as the nearness of at least 2 red blood cells for each high powerful field (HPF) recognized by routine urine assessment for diseases superfluous of the urinary tract [2]. Two types of erythrocytes can be found in the urine

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sediment; isomorphic (fresh) and dysmorphic (distorted) erythrocytes, indicating glomerular or non-glomerular hematuria [3]. Hematuria is a pervasive condition that is described by the presence of erythrocytes in the urine. Completely, it is classified into microscopic and macroscopic (gross) hematuria. In microscopic hematuria, there is no optical indication of the presence of blood unless the urine deposit viewed microscopically [4]. Hematuria might be viewed as transient because of contaminations, injury, fever, sex, and exercise which are normally microscopic (benign). Persistent hematuria and its side effects might be related to some efficient sicknesses, for example, hypertension, diabetes, and renal illness [5] and is isolated into hematuria of glomerular and non-glomerular sources [6]. As for glomerular hematuria, the assortment of urinary red cells fit as a fiddle are expanded, and such the red blood cell is generally called distorted or dysmorphic red blood cells (dRBCs). The precise pathological mechanism of an arrangement of dRBCs is not completely comprehended. In any case, it is proposed that dRBCs are erythrocyte, which leaked via the defected glomerular and were harmed by osmotic affected or mechanically during their entry to the tubular system of the renal particularly the collecting duct. In opposite, in non-glomerular hematuria, urinary erythrocyte has an increasingly uniform morphology with the goal that it is called isomorphic RBCs [7]. Urine examination is as yet thought about a significant diagnostic tool for nephrologists. In general practice, the morphology of urinary erythrocyte has been supported as a fine diagnostic to recognize glomerular and non-glomerular reasons for hematuria [7]. The diagnosis of hematuria can be carried out by urine dipstick which is sensitive for detecting red blood cells (RBCs) in mm^3 and give positive results in the presence of hemoglobinuria and/or myoglobinuria, and negative results with reddish urine due to drugs or food [2]. This study was led to find out the indication of erythrocyturia and other outcomes for hematuria.

2. Material and Methods

2.1. Study Design and Participants

A cross-sectional investigation was performed on patients aged between 3 and 90 years and being surveyed in the Dr. Awaad Medical Center. The examination was directed from June 2017 to July 2018 on the attended individuals who were screened for eligibility, 170 consecutive individuals with hematuria were enrolled. Urinalysis used as both a screening and a demonstrative. Patients with proteinuria of abundance than 0.5g/24hours or treated with Propofol, chlorpromazine, Thioridazine, and Ex-lax or had Porphyria, Sickle cell anemia, Bladder cancer, and Nephrolithiasis, were avoided.

2.2. Study Classification

According to the American Urological Association (AUA) best practice policy recommendation, hematuria was classified into; microscopic hematuria, macroscopic (gross) hematuria, and isolated hematuria.

2.3. Study Technique

Midstream fresh urine samples were gathered in a clean container (50 ml capacity) from each patient. For women, we advised them to clean the external genitalia (front to back) before voiding the urine to avoid contamination with secretions. The urine samples were analyzed within 30 – 60 minutes after the patient voids. The analytical performance was conducted in 3 parts. First, a gross view inspection of the urine sample to determine color and turbidity. Second, the urine specimen undergoes chemical detection by using urine dipstick. This step was performed on the uncentrifuged urine sample. The test strips are submerged into the urine, then analyzed and compared with controls. Third, the urine samples were centrifuged at 3000 revolutions per minute (RPM) for 3 – 5 minutes and the supernatant transferred to another test tube for checking albumin by Sulfosalicylic acid (SSA). The residual pellet is resuspended and fewer amounts of the deposit poured onto the slide. This sediment was then examined microscopically for components such as pus cells, casts, crystals, and ova. These elements in the urine deposit are usually reported as the number viewed per LPF (100x) or HPF (400x). All dRBCs observed in 10 -12/HPF were counted in each case to determine the proportion of distorted RBCs. Urinary dysmorphic erythrocytes were defined depending on the criteria as reported formerly [6]. Briefly, the dRBCs illustrated irregular membranes or little surface blebs and showed vesicular shape. Hematuria belonged to glomerular source demonstrates a pleomorphic aspect and erythrocytic casts can existed. In this report, although we have enumerated the dRBCs we did not discriminate between the different types of distorted erythrocytes. Urine examinations were performed by an expert laboratory hematologist.

2.4. Study Evaluation

The appraisal consisted of social-demographic, history, smoking, urinalysis, and blood test if indicated. Physical properties of urinary examination were performed semi-quantitatively by (DUS GK, DFI CO., Ltd, Korea) and ascertained by microscopic evaluation. Determination of hematuria degree was performed by enumerating the number of red blood cells (RBCs) (fresh (f) = isomorphic or dysmorphic=d) seen per high power field (HPF) (400 x) in urine sediment after centrifugation according to the national committee for clinical laboratory standards (NCCLS)

recommendations [8]. Hematuria was scored in +, ++, and +++ corresponding to 2 – 20, 21 – 100, and > 100 erythrocyte/ μ l, respectively [6]. Proteinuria was performed using two quantitative methods of measurement, (Albustix, DUS GK) which is more sensitive in detecting albumin. The other measurement is the SSA (3 parts of 3% SSA with the one-part urine supernatant) which is a confirmatory test for the presence of albumin (sensitive to detect 5 – 10 mg/dl of protein), the protein score evaluated as: Trace = 20 mg/dl, 1+ = 50 mg/dl, 2+ = 200 mg/dl, 3+ = 300 mg/dl, and 4+ = \geq 1000 mg/dl. Urinary PH was estimated by a semi-quantitative (DUS GK, DFI CO., Ltd, Korea). Serum creatinine and blood urea were measured to evaluate the renal function of each individual. Renal ultrasonography was reserved for patients without recognition of the causes of hematuria.

2.5. Model Scoring Protocol

A scoring scheme based on (< 3, 3 – 10, and > 10 RBC/HPF), < 3 recognized normal and the other each provides a score of 0, 1, 2, 3, respectively. RBC with Proteinuria < 2 g/dl (score 0), subtended > 2 g/dl (score 1), 3 – 10 RBC with > 2 g/dl proteinuria indicates (score 2), score 3 indicating > 10 RBC/HPF and \geq 2 g/dl of proteinuria [9].

2.6. Statistical Analysis

Data were displayed as mean \pm SD unless otherwise specified Chi-square test was used in the comparison of data as appropriate. The mean dRBCs in the four diagnostic groups were compared using one-way ANOVA. The level of albuminuria and the urinary dRBCs were compared using the Fisher exact test. Pearson's bivariate correlation was also measured. Analyses were performed by statistical package for the social sciences software (SPSS 24, IBN, Chicago, USA) for windows 10. The sensitivity, specificity, positive predictive value, and negative predictive value relevant to dRBCs and fRBCs were also assessed by diagnostic test evaluation (MedCalc version 16.8, easy-to-use statistical software).

2.7. Ethics Approval

Approval of this study was elicited from the Dr. Awaad medical center, and ministry of health issued by the local ethical committee, Red Sea State, Sudan. Written consent was taken from each participant. A parent/guardian also was signing the main consent on behalf of each child in this study.

3. Results

In this report, 170 consecutive patients presenting with hematuria were enrolled. 121 (71.2%) were males and 49

(28.8%) were females, with a mean age of (40.4 \pm 16.5 years). The mean creatinine level in the patient's serum was 0.91 \pm 0.32 mg/dl (range 0.42 – 2.56). All characteristics of the patients are listed in Table 1.

3.1. Semi-quantitative Urinalysis

Hematuria was present in the patients as the following frequencies; + in 110 (64.7%), ++ in 50 (29.4%), and +++ in 10 (5.9%). Proteinuria was observed in 145/170 (73.5%) of the patients with hematuria and albuminuria levels were statistically significant with hematuria (P < 0.000) (Table 2). The mean urinary PH of samples included in this report was 6.0.

3.2. Microscopic Examination of Urinary Sediment

The examination of urine deposits demonstrated a mean \pm SD of 16.6 \pm 23.3 dysmorphic red blood cells/HPF. dRBCs were encountered in 122/170 (71.8%) (P < 0.000) of an entire group of patients with hematuria. The mean \pm SD of the isomorphic red cell was 12.0 \pm 20.5 red cells/HPF. fRBCs were also detected in 99/170 (58.2%) (P < 0.000) of an entire group of patients with hematuria. Interestingly, urinary casts were presented in 63/170 (37%); 8/170 (4.7%) cellular cast, 27/170 (15.9%) granular cast, 5/170 (2.9%) hyaline cast, 11/170 (6.5%) cellular + granular casts, 4/170 (2.4%) granular + hyaline casts, and 8/170 (4.7%) erythrocytes cast. In addition, urinary crystals were found in the 54/170 (31.8%); 5/170 (2.9%) uric acid crystal, 38/170 (22.4%) calcium oxalate, 9/170 (5.3%) amorphous urate, and 2/170 (1.2%) amorphous phosphate. However, there was an insignificant association of hematuria with casts and crystals (P < 0.055 and 0.052, respectively) (Table 2).

3.3. Diagnostic Performance of Hematuria

All of the patients were classified into four groups according to the American Urological Association guidelines. 10/170 (5.9%) had gross hematuria, 49/170 (28.8%) had microscopic hematuria with clinical symptoms, 56/170 (32.9%) had microscopic hematuria with proteinuria, and 55/170 (32.4%) had isolated hematuria. Citing the present findings, clinical manifestations, and renal ultrasonography reports, the patients were diagnosed for the causes of hematuria (Table 1). The overwhelming majority outcomes of hematuria in this report were among the urinary tract infection (UTI) (37.6%), followed by glomerulonephritis (19.5%), cystitis (18.2%), pyelonephritis (10.0%), and renal stones (7.6%). In other words, 72.9% of patients had hematuria due to non-glomerular causes and 19.5% of patients had hematuria due to glomerular causes. Foul-smelling was considered the only

clinical remark that had important significance with the four groups of hematuria ($P < 0.001$) and with the causes of hematuria ($P < 0.018$). During the study, 14 patients (8.2%) had hypertension, 11 patients (6.5%) had diabetes, 8 patients (4.7%) had diabetes along with hypertension, and 13 patients (7.6%) had other chronic diseases. Unexpectedly, these chronic diseases were insignificant with hematuria ($P < 0.241$).

Overall, of 170 patients, 50 (29.4%) had > 16.6 dRBCs and 47 (27.6%) had ≥ 12.0 fRBCs. Table 3 offered the diagnostic performance values of glomerular disease (GD), glomerulonephritis, non-glomerulonephritis, and non-glomerular disease. Therefore, dRBCs were significantly different with albuminuria and strongly significant with the causes of hematuria at the time of the study ($P < 0.005$ and 0.000 , respectively). In contrast, the urinary dRBCs was insignificant with smoking and chronic disease association ($P < 0.630$ and 0.473 , respectively). The presence of urinary dRBCs varied significantly between the four classified groups and was highest in the group with microscopic hematuria with proteinuria ($P < 0.000$; Table 4). Urinary dysmorphic red cells were negatively correlated with age and sex ($r = 0.29/ P < 0.705$, $r = - 0.12/ P < 0.126$, respectively). The urinary dRBC was observed in UTI as 42/170 (24.7%), in glomerulonephritis as 28/170 (16.5%), in pyelonephritis as 12/170 (7.1%), and in renal stone as 7/170 (4.1%). Albuminuria was also significantly different from the four groups of hematuria ($P < 0.000$), but serum creatinine levels were insignificant ($P < 0.134$).

3.4. Diagnostic Findings of dRBCs and fRBCs

The presence of hematuria had 66.7% sensitivity and 68.8% specificity for glomerular disease. The infestation of dRBCs > 16.6 was indicative of the presence of any glomerular, with a positive predictive value (PPV) of 90.2% and negative predictive value (NPV) of 32.4%. Side by side, the existence of > 12.0 of fRBCs was sensitive (91.9%) but less specific (64.0%) for the presence of glomerular origin, with PPV of 92.7% and NPV of 61.5% (Table 5). A model score protocol was constructed based on the analysis of assembled hematuria and proteinuria. In score 0 (no hematuria or < 2 g/dl proteinuria) the eventuality of the presence of GD was 12.5%. Respect to score 1, the eventuality of GD was 27.1%, with increased to 35.4% in score 2. In score 3 (> 10 RBCs/HPF and ≥ 2 g/dl proteinuria) the probability of having GD was 25% ($P < 0.001$). Therefore, non-GN was identified to having a score 0 (35.4%), score 1 (38.9%), score 2 (19.2%), and score 3 (6.2%) ($P < 0.001$) (Figure 1).

Table 1. Characteristics of the patients with hematuria.

Characteristics	Patients ($n=170$)
Age (mean \pm SD)	40.4 \pm 16.5 years
(range)	3 – 90 years
Sex (male)	121 (71.2%)
(female)	49 (28.8%)
Demographic data	
<i>Tribes</i>	
Eastern Sudan tribes	71 (41.8%)
Northern Sudan tribes	69 (40.6%)
Western Sudan tribes	17 (10.0%)
Immigrants	13 (7.6%)
<i>Residence</i>	
Downtown area	33 (19.4%)
Eastern area	72 (42.4%)
Southern area	65 (38.2%)
<i>Smoking</i>	
Smoker	36 (21.2%)
Non-smoker	128 (75.3%)
Ex-smoker	6 (3.5%)
Clinical manifestations	
Urgency	78 (45.9%)
Strangury	54 (31.8%)
Frequent urination	66 (38.8%)
Burning micturition	91 (53.5%)
Suprapubic pain	37 (21.8%)
Foul smelling	57 (33.5%)
Dysuria	48 (28.2%)
Loin pain	64 (37.6%)
Low grade fever	45 (26.5%)
Causes of Hematuria	
UTI	64 (37.6%)
Cystitis	31 (18.2%)
Glomerulonephritis	20 (11.8%)
Pyelonephritis	17 (10.0%)
Nephrotic syndrome	2 (1.2%)
Viral hemorrhagic fever	4 (2.4%)
Benign Prostatic Hypertrophy	4 (2.4%)
Renal stones	13 (7.6%)
Pelvic inflammatory disease	2 (1.2%)
Malaria	1 (0.6%)
Hemorrhoid	1 (0.6%)
Nephritic syndrome	11 (6.5%)
A disease associated	
Hypertension (HTN)	14 (8.2%)
Diabetes mellitus (DM)	11 (6.5%)
HTR + DM	8 (4.7%)
Other diseases	13 (7.6%)
No disease	124 (72.9%)

Table 2. Findings of the studied patients with hematuria.

Parameters	Hematuria (n=170)			P. value	
	+ (n=110)	++ (n=50)	+++ (n=10)		
dRBCs					
Nil	34 (30.9%)	10 (20.0%)	4 (40.0%)	0.000	
+	76 (69.1%)	7 (14.0%)	0 (0.0%)		
++	0 (0.0%)	33 (66.0%)	0 (0.0%)		
+++	0 (0.0%)	0 (0.0%)	6 (60.0%)		
fRBCs					
Nil	51 (46.4%)	14 (28.0%)	5 (50.0%)	0.000	
+	59 (53.6%)	14 (28.0%)	0 (0.0%)		
++	0 (0.0%)	22 (44.0%)	0 (0.0%)		
+++	0 (0.0%)	0 (0.0%)	5 (50.0%)		
Albuminuria					
Nil	41 (37.3%)	3 (6.0%)	0 (0.0%)	0.000	
Trace	45 (40.9%)	19 (38.0%)	1 (10.0%)		
+	16 (14.5%)	19 (38.0%)	2 (20.0%)		
++	7 (6.4%)	6 (12.0%)	6 (60.0%)		
+++	0 (0.0%)	2 (4.0%)	1 (10.0%)		
++++	1 (0.9%)	1 (2.0%)	0 (0.0%)		
Urinary casts					
Cellular cast	3 (2.73%)	4 (8.0%)	1 (10.0%)	0.055	
Granular cast	16 (14.6%)	8 (16.0%)	3 (30.0%)		
Hyaline cast	3 (2.73%)	2 (4.0%)	0 (0.0%)		
Cellular + granular	4 (3.6%)	7 (14.0%)	0 (0.0%)		
Granular + hyaline	3 (2.73%)	1 (2.0%)	0 (0.0%)		
Erythrocytic cast	2 (1.82%)	5 (10.0%)	1 (10.0%)		
Nil	79 (71.8%)	23 (46.0%)	5 (50.0%)		
Urinary crystals					
Uric acid	4 (3.6%)	1 (2.0%)	0 (0.0%)		0.052
Calcium oxalate	32 (29.1%)	6 (12.0%)	6 (60.0%)		
Amorphous urate	5 (4.6%)	2 (4.0%)	2 (20.0%)		
Amorphous phosphate	2 (1.8%)	0 (0.0%)	0 (0.0%)		
Nil	67 (60.9%)	41 (82.0%)	2 (20.0%)		

dRBCs; dysmorphic red cells, fRBCs; fresh red cells

Table 3. Pathologic diagnosis and the values of dRBCs and fRBCs in common entities.

Type of disease	n (%) of total group	n (%) of patients with > 16.6 dRBCs	n (%) of patients with > 12.0 fRBCs
Glomerular disease (GD)	46 (27.1%)	23 (50%)	18 (39.1%)
Glomerulonephritis (GN)	20 (11.8%)	12 (60%)	6 (30%)
Nephrotic syndrome	2 (1.2%)	1 (50%)	1 (50%)
Nephritic syndrome	11 (6.5%)	9 (81.8%)	5 (45%)
Renal stone	13 (7.6%)	1 (7.7%)	6 (46%)
Non-GN	114 (67.0%)	24 (21.1%)	24 (21.1%)
UTI	64 (37.6%)	7 (10.9%)	9 (14.1%)
Cystitis	31 (18.2%)	7 (22.6%)	8 (25.8%)
Pyelonephritis	17 (10.0%)	10 (58.8%)	7 (41.2%)
Pelvic Inflammatory disease	2 (1.2%)	0 (0.0%)	0 (0.0%)
Non-GD	10 (5.9%)	3 (30%)	5 (50%)
Viral hemorrhagic fever	4 (2.4%)	2 (50%)	2 (50%)
Malaria	1 (0.6%)	0 (0.0%)	1 (100%)
Hemorrhoid	1 (0.6%)	0 (0.0%)	1 (100%)
Benign prostatic hypertrophy	4 (2.4%)	1 (25.0%)	1 (25.0%)

, GD: glomerular disease, GN; glomerulonephritis

Table 4. Clinical findings at the time of presentations with the diagnostic hematuria groups.

Diagnostic group	Gross Hematuria (n=10)	Microscopic hematuria with clinical symptoms (n=49)	Microscopic hematuria with proteinuria (n=56)	Isolated Hematuria (n=55)	P. value
Sex (males)	7 (70%)	35 (71.4%)	42 (75%)	37 (67.3%)	0.849
(females)	3 (30%)	14 (28.6%)	14 (25%)	18 (32.7%)	
Serum Creatinine (0.4-1.6 mg/dl)					
Normal levels	10 (5.9%)	48 (28.2%)	52 (30.6%)	55 (32.4%)	0.134
Abnormal levels	0 (0.0%)	1 (0.6%)	4 (2.4%)	0 (0.0%)	
Albuminuria					

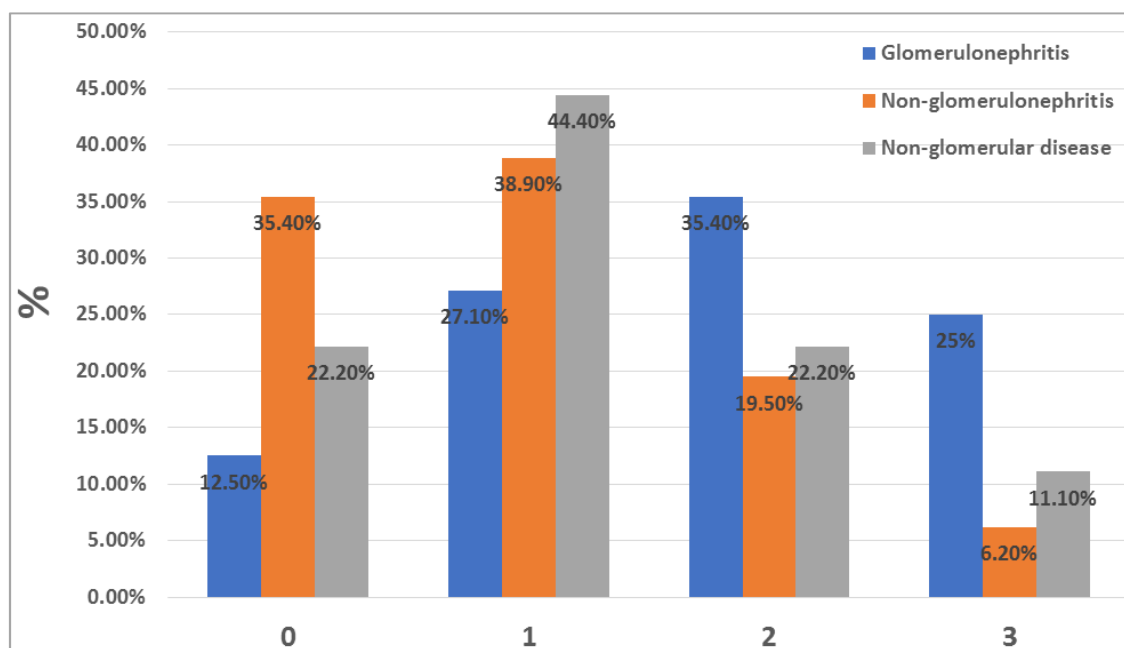
Diagnostic group Characteristic data	Gross Hematuria (n=10)	Microscopic hematuria with clinical symptoms (n=49)	Microscopic hematuria with proteinuria (n=56)	Isolated Hematuria (n=55)	P. value	
Nil	0 (0.0%)	3 (6.1%)	0 (0.0%)	41 (74.6%)	0.000	
Trace	2 (20.0%)	30 (61.2%)	19 (33.9%)	14 (25.4%)		
+	1 (10.0%)	16 (32.7%)	20 (35.7%)	0 (0.0%)		
++	5 (50.0%)	0 (0.0%)	14 (25.0%)	0 (0.0%)		
+++	2 (20.0%)	0 (0.0%)	1 (1.8%)	0 (0.0%)		
++++	0 (0.0%)	0 (0.0%)	2 (3.6%)	0 (0.0%)		
Hematuria						
1+	0 (0.0%)	37 (75.5%)	21 (37.5%)	52 (94.6%)	0.000	
2+	4 (40.0%)	11 (22.5%)	32 (57.1%)	3 (5.4%)		
3+	6 (60.0%)	1 (2.0%)	3 (5.4%)	0 (0.0%)		
dRBCs						
Nil	2 (20.0%)	15 (30.6%)	11 (19.6%)	20 (36.4%)	0.000	
+	0 (0.0%)	26 (53.1%)	23 (41.1%)	34 (61.8%)		
++	4 (40.0%)	7 (14.3%)	21 (37.5%)	1 (1.8%)		
+++	4 (40.0%)	1 (2.0%)	1 (1.8%)	0 (0.0%)		
Causes of hematuria						
UTI	1 (10%)	21 (42.9%)	14 (25%)	28 (50.9%)	0.001	
Cystitis	0 (0.0%)	8 (16.3%)	8 (14.3%)	15 (27.3%)		
Glomerulonephritis	4 (40%)	5 (10.2%)	10 (17.9%)	1 (1.8%)		
Pyelonephritis	1 (10%)	5 (10.2%)	8 (14.3%)	3 (5.5%)		
Nephrotic syndrome	0 (0.0%)	0 (0.0%)	2 (3.6%)	0 (0.0%)		
Viral hemorrhagic fever	0 (0.0%)	3 (6.1%)	1 (0.0%)	0 (0.0%)		
Prostatic enlarged	1 (10%)	0 (0.0%)	1 (1.8%)	1 (1.8%)		
Renal stones	0 (0.0%)	3 (6.1%)	6 (10.7%)	4 (7.8%)		
Pelvic inflammatory	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (3.6%)		
Malaria	0 (0.0%)	1 (2.0%)	0 (0.0%)	1 (1.8%)		
Hemorrhoid	0 (0.0%)	0 (0.0%)	1 (1.8%)	0 (0.0%)		
Nephritic syndrome	3 (30%)	3 (6.1%)	5 (8.9%)	0 (0.0%)		
Urgency						0.669
Present	4 (40.0%)	26 (53.1%)	25 (44.6%)	23 (41.8%)		
absent	6 (60.0%)	23 (46.9%)	31 (55.4%)	32 (58.2%)		
Strangury					0.760	
Present	4 (40.0%)	17 (34.7%)	15 (26.8%)	18 (32.7%)		
absent	6 (60.0%)	32 (65.3%)	41 (73.2%)	37 (67.3%)		
Frequent urination					0.060	
Present	5 (50.0%)	18 (36.7%)	15 (26.8%)	28 (50.9%)		
absent	5 (50.0%)	31 (63.3%)	41 (73.2%)	27 (49.1%)		
Burning micturition					0.732	
Present	4 (40.0%)	26 (53.1%)	29 (51.8%)	32 (58.2%)		
absent	6 (60.0%)	23 (46.9%)	27 (48.2%)	23 (41.8%)		
Suprapubic pain					0.307	
Present	2 (20.0%)	11 (22.4%)	8 (14.3%)	16 (29.1%)		
absent	8 (80.0%)	38 (77.6%)	48 (85.7%)	39 (70.9%)		
Foul smelling					0.001	
Present	6 (60.0%)	16 (32.7%)	27 (48.2%)	8 (14.5%)		
absent	4 (40.0%)	33 (67.3%)	29 (51.8%)	47 (85.5%)		
Dysuria					0.786	
Present	3 (30.0%)	16 (32.7%)	16 (28.6%)	13 (23.6%)		
absent	7 (70.0%)	33 (67.3%)	40 (71.4%)	42 (76.4%)		
Loin pain					0.518	
Present	6 (60.0%)	18 (36.7%)	20 (35.7%)	20 (36.4%)		
absent	4 (40.0%)	31 (63.3%)	36 (64.3%)	35 (63.6%)		
Low grade fever					0.147	
Present	1 (10.0%)	15 (30.6%)	19 (33.9%)	10 (18.2%)		
absent	9 (90.0%)	34 (69.4%)	37 (66.1%)	45 (81.8%)		

UTI; urinary tract infection, dRBCs; dysmorphic red cells

Table 5. dRBCs and fRBCs performance for diagnosis glomerular vs non-glomerular.

Parameters	Sensitivity %	Specificity %	PPV	NPV	95% CI
DRBCs					
GD	66.7%	68.8%	90.2%	32.4%	81.4 – 95.1
Non-GN	55.9%	28.2%	57.6%	26.8%	53.5 – 61.6
Non-GD	58.8%	50.0%	76.9%	30.0%	57.7 – 89.1
FRBCs					
GD	82.1%	47.1%	71.9%	61.5%	64.5 – 78.2
Non-GN	91.9%	64.0%	92.7%	61.5%	88.2 – 95.5
Non-GD	90.9%	50.0%	66.7%	83.3%	51.1 – 79.3

GD: glomerular disease, GN; glomerulonephritis, PPV; positive predictive value, NPV; negative predictive value.

**Figure 1.** A score scheme exhibited the probability for glomerular vs non-glomerular.

4. Discussion

Hematuria is a common demonstrative phenomenon in clinical practice. Despite the validity of a sensitive dip-stick for urinalysis, the patients are still referred for microscopical investigation of hematuria. Moreover, there remains controversy in the literature regarding the degree of hematuria, which is a cause of concern [1]. This report included 170 patients presented with hematuria to measure dysmorphic and isomorphic red cells as diagnostic values that assist to identify the origin of red cells and therefore useful in the urology department to determine glomerular diseases. However, patients with gross and/or microscopic hematuria should be referred to urology for more investigations.

There is a concordance amongst experts that gross hematuria is a disturbing presentation and ensures an exhaustive investigation [10]. In fact, overt blood in the urine is thought to be the initial presentation in 40% and 85% of patients with renal and bladder cancers, respectively. These findings are completely different from our results because they do not

conform to the study criteria. In this examination, 37.6% of patients had urinary tract contamination, which is a demonstrated urological pathology. These patients were a lot more seasoned contrasted with the patients in the other symptomatic causes. This reality is reliable with Grossfeld *et al* and Crop *et al* [6, 11]. In this work, we found that the significant presence of dRBCs > 16.6 RBC/HPF indicates that dRBCs are quite specific for the glomerular disease compared with a non-glomerular origin. The outcome of dRBCs > 16.6 RBC/HPF prominent in a urine specimen exhibited high specificity and high PPV for the diagnosis of glomerular disease with optimized when proteinuria was associated. Thus, the finding of fRBCs > 12.0 RBC/hpf showed high sensitivity and high PPV for the distinguishing of non-glomerulonephritis. Scoring protocol for anticipated the presence of glomerular disease based on both proteinuria and hematuria had the predictive choice for glomerular disease. In the present study, patients with the score 0 had a 12.5% prospect of having a glomerular disease. The hazard of the glomerular disease continued to rise until score 3. A similar determination was provided previously by Hamadah *et al* [9]. Established on our outcome, we set up that age and

sex did not redound to the nearness of dRBCs. Also, the clinical appearances related to this work were noted insignificant except the foul-smelling which is showing a typical indication seamed with hematuria.

A previous study suggested that identifying $\geq 40\%$ dRBCs in urine deposit may reject urological pathology. As it were, this line of thinking has been arranged that the patients with overabundance than 40% urinary dRBCs ought to be raised to a nephrologist [12]. The pathophysiology of the increasing percentage of dRBCs in patients with urological sources of hematuria is uncertain, as the dRBCs are presumed to be formed in the tubular system of the kidney due to mechanical and/or osmotic alteration and not in the lower urinary tract [6]. The plausible clarification for the relative augmentation in the level of dRBCs in these patients could be the concurrence of glomerular sickness [13]. Nevertheless, these discoveries are extensively like our outcomes that most had $< 40\%$ urinary dRBCs and proven urological pathology. Unfortunately, a renal biopsy was not borne in these patients. In the conclusion of these cases, we depended exclusively on renal ultrasonography. Over the span of this examination, 46 patients (27.1%) with demonstrated urological issues created glomerular sickness in spite of the nearness of > 16.6 RBC/HPF of dRBCs in their urine deposits. This recommends the presence of urinary dRBCs is generally valuable to advert glomerular issue, however, may keep out glomerular sickness in patients with a urological issue.

The recurrence of urinary dRBCs was fundamentally expanded in patients with a glomerular issue in correlation with patients with urological illness [6]. In any case, a diminished % dRBCs did not preclude glomerular issues as the level of dRBCs ranged between 1 – 50%. Albuminuria is a significant estimation of glomerular harm and was fundamentally present in patients with demonstrated glomerular hematuria [14]. Serum creatinine levels as a gauge of glomerular filtration rate (GFR) could likewise be an analytic tool of the glomerular disorder. However, in this report, there was an insignificant association between serum creatinine levels and the groups of hematuria. In the 2 patients with nephrotic syndrome, abnormal creatinine levels were accounted for in a relationship with ≥ 100 urinary dRBCs and stamped albuminuria. Then again, 11 patients with the nephritic syndrome had remarked erythrocytic casts, albuminuria, and > 16.6 RBC/HPF of urinary dRBCs. These patients would not have been diagnosed by the presence of urinary dRBCs alone alternatively they were considered types of glomerular disease. The urinary red cell casts regarded to be a virtual pathognomic of glomerular bleeding [15]. In this context, erythrocyte casts have existed in 37% of patients with hematuria, this finding was higher than the previously noted [9]. Furthermore, it very well may be

accepted that utilizing dRBCs, erythrocyte scores on the dipstick, proteinuria score, serum creatinine, and significant presentation of erythrocyte casts can raise the affectability sign of the glomerulopathy.

Many limitations have been demonstrated in the present study. We did not address the PH of the urine sample; the acidic PH may have effects on both the dRBCs and erythrocytic casts that are encountered in more acidic urine. So, we did not care and no precaution was made to estimate the concentration of the urine osmolality, which may affect the dRBCs and red cell casts. Unfortunately, due to short facilities, we did not use a renal biopsy or computed tomography (CT) scan for evaluating glomerular disease. Likewise, we did exclude another strategy for evaluating the urinary dRBCs such as an electron microscope. Manual microscopic evaluation is still considered routinely to identify the different cell types [16]. Nonetheless, further appraisal ought to be seen with different strategies, ideally with the enormous examination populace.

5. Conclusion

To finish up, our discoveries obviously show that the presence of > 16.6 RBC/HPF of urinary dysmorphic RBCs was a significant prognostic for a glomerular disorder, only combined with proteinuria it is a specific indication of glomerular origin. fRBCs were anticipated to the non-glomerular origin. This report also reveals the significance of dRBCs in isolated hematuria. Dysmorphic RBCs that persist in healthy subjects denote a glomerular source. UTI, glomerulonephritis, and cystitis were considered the prevalent outcomes of hematuria in this report.

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Authors' Contributions

BA contributed in literature search and manuscript writing. BA had the main idea of the study and contributed in manuscript writing; MA contributed to Dr. Awaad medical clinic work. BA and MO contributed in statistical analysis. MO and BA supervised the study & critically reviewed the manuscript. All authors read and approved the final draft of the manuscript.

Competing Interests

The authors declare that they have no competing interests.

References

- [1] Yafi FA, Aprikian AG, Tanguay S, Kassouf W. Patients with microscopic and gross hematuria: practice and referral pattern among primary care physicians in a universal health care system. *Can Urol Assoc J.* 2011; 5 (2): 97 – 01.
- [2] Koo KC, Lee KS, Choi AR, Rha KH, Hong SJ, Chung BH. Diagnostic impact of dysmorphic red cells on evaluating microscopic hematuria: the urologists perspective. *Int Urol Nephrol.* 2016; 48 (7): 1021 – 7.
- [3] Tesser Poloni J, Bosan IB, Garigali G, Fogazzi GB. Urinary Red Blood Cells: not only Glomerular or non-glomerular. *Nephron Clin Pract* 2012; 120: c36–c41.
- [4] Sultana T, Sultana T, Rahman MQ, Ahmed ANN Evaluation of Hematuria and use of phase contrast microscope: A short review. *J Dhaka Med Coll.* 2011; 20 (1): 63 – 7.
- [5] Feld LG, War WR, Perez LM, Joesph DB. Hematuria. An Integrated medical and surgical approach. *Pediatr CLi North Am.* 1997; 44 (5): 1191 – 210.
- [6] Crop MJ, de Rijke YB, Verhagen PC, Crnsberg K, Zietse R. Diagnostic value of urinary dysmorphic erythrocyte in clinical practice. *Nephron Clin Pract.* 2011; 115: c203-c212.
- [7] Cohen RA, Brown RS. Microscopic hematuria. *N Engl J Med.* 2003; 2330-2337.
- [8] Fogazzi GB, Edefonti A, Garigali G, Giani M, Zolin A, Raimondi S, Mihatsch MJ, Messa P: Urine erythrocyte morphology in patients with microscopic haematuria caused by a glomerulopathy. *Pediatr Nephrol.* 2008; 23: 1093–1100.
- [9] Hamadah AM, Gharaibeh K, Mara KC, Thompson KA, Lieske JC, Said S et al. Urinalysis for the diagnosis of glomerulonephritis: role of dysmorphic red blood cells. *Nephrol Dial Transplant.* 2018; 33 (8): 1397-1403.
- [10] Wollin T, Laroche B, Posy K. Canadian guidelines for management of asymptomatic microscopic hematuria in adults. *Can Urol Assoc J.* 2009; 3: 77-80.
- [11] Grossfeld GD, Litwin MS, Wolf JS, Hricak H, Shuler CL, Agerter DC, Carroll PR: Evaluation of asymptomatic microscopic hematuria in adults: The American Urological Association best practice policy-part I: definition, detection, prevalence, and etiology. *Urology.* 2001; 57: 599 -603.
- [12] Huussen J, Koene RA, Meuleman EJ, Hilbrands LB: Diagnostic approach in patients with asymptomatic haematuria: efficient or not? *Int J Clin Pract.* 2006; 60: 557–561.
- [13] Wang YY, Savige J: The epidemiology of thin basement membrane nephropathy. *Semin Nephrol.* 2005; 25: 136–139.
- [14] Dong ZY, Wang YD, Qiu Q, Kai H, Zhang L, Wu J, Zhu HY et al. Dysmorphic erythrocytes are Superior to hematuria for indicating non-diabetic renal disease in type 2 diabetics. *J Diabetes Investig.* 2016; 7 (1): 115-20.
- [15] Chu-Su, Y, Shukuya K, Yokoyama T, Lin WC, Chiang CK, Lin CW. Enhancing the Detection of Dysmorphic Red Blood Cells and Renal Tubular Epithelial Cells with a Modified Urinalysis Protocol. *Sci. Rep.* 2017; 7: 40521.
- [16] Shayanfar N, Tobler U, von Eckardstein A, Bestmann L: Automated urinalysis: first experiences and a comparison between the IriSiQ200 urine microscopy system, the Sysmex UF-100 flow cytometer and manual microscopic particle counting. *Clin Chem Lab Med* 2007; 45: 1251–1256.