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ORIGINAL ARTICLE

The Study of the Value of Mean Corpuscular Volume in the Urine Red Blood Cell Phase in the Differential Diagnosis of Hematuria

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ABSTRACT **Objective:** The changes of urinary red blood cell morphology and the average volume of red blood cell were examined by MCV. **Method:** In 100 cases of patients with urinary sediment microscopy of hematuria, and used blood cell analyzer for determination for MCV in urinary RBC. **Results:** Renal hematuria MCV and the outer peripheral blood MCV has significant difference ($p < 0.01$) and non-renal hematuria and peripheral blood MCV had no significant difference, glomerular hematuria and non-glomerular hematuria erythrocyte deformity was significantly different ($p < 0.01$), renal hematuria MCV is less than or equal to 73 fL, abnormal red blood cells with 2 or more, deformity rate is more than or equal to 76%. **Conclusion:** RBC phase combined with MCV detection of urine RBC is the practical value in diagnosis of glomerular hematuria.

KEYWORDS
Hematuria
Urine RBC
MCV

1. Introduction

In this paper, 100 patients with hematuria were examined by blood cell analyzer and phase contrast microscope to investigate the diagnostic value of urinary system disease.

2. Materials and methods

2.1. Specimens selection

100 hospitalized patients which, 50 cases of renal glomerular nephritis from the Department of internal medicine of our hospital, and the remaining non renal hematuria for patients with trauma. The urine samples of the patients with glomerulonephritis and non-glomerular nephritis were collected for 1 hour. 10 mL of urine was span with 1500 rpm for 10 minutes. Discard the supernatant and leaving 0.5 mL for reserve.

2.2. Instruments and reagents

US OLYMP phase contrast microscope and Smix XT-1800i Sy blood analyzer.

2.3. Experimental method

Sterile urine cup was used to collect the urine of patients. 10 mL of the urine was underwent centrifugation with 1500 rpm for 5 min. The samples of urine in the blood cell analyzer, was process by serial dilution for the determination of urine red blood cells MCV. All the determination was done in 1 hour.

2.4. Diagnostic criteria

The morphology of urinary red blood cells were classified according to the red blood cell (G) and non-renal red blood cells (N). Class G of red blood cell (RBC) five type (G1–G5) features are as follows: G1 with spores or pseudopodium projection, and can be various in size, it come with the shape of doughnuts, spherical, lip, or ring; when hemoglobin is lost with spores, small pseudopods or a small circle of the double ringed or loop like structures will form; G2 red cells were spherical, small mouth, small annular; G3 is like bread cycle, target shape; G4 showed circular or granules on cell surface deposition; G5 is irregular, broken, cracked shape, shedding spores and cell debris. For renal hematuria, Class G of red blood cell in urine accounted for total red blood cell count is greater than or equal to 76%, for non-renal hematuria less than or equal to 20% ,and for mixed hematuria the range is between 20–80% [1]. MCV

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was measured by blood cell analyzer, and the critical value of RBC was less than 75 fL, and 75 fL was non glomerular hematuria.

3. Results

Table 1 show the MCV value of glomerular nephritis group was much less than that of peripheral blood MCV value. There was no significant difference in between ($p < 0.01$) and peripheral blood MCV. While there was two cases of glomerular nephritis and non-glomerular nephritis with significantly different ($p < 0.01$). 43 cases of renal hematuria in patients with glomerular hematuria, 41 cases with oval shape, spine, and polygon shape of red blood cells. In 57 cases of non-glomerular hematuria, 53 cases of red blood cells were homogeneous, and the diagnostic accuracy was 92.9%.

Table 1. Glomerular nephritis and non-renal hematuria in patients with hematuria, as well as the control of the MCV findings.

Project	Cases	MCV (fL)	Erythrocyte deformity (%)
Glomerular hematuria	43	66.3 ± 6.1	81.5 ± 4.9
Non glomerular hematuria	57	89.2 ± 5.9	22.2 ± 8.1
Peripheral blood	100	92.5 ± 7.8	-

The sensitivity, specificity and accuracy of the ROC curves are used to determine the optimal threshold value. Urine MCV is less than or equal to 70 fL to distinguish glomerular hematuria with sensitivity of 80.6%, specificity of 90.4% and accuracy of 86.6%; urine MCV is less than or equal to 75 fL sensitivity for 90.3%, especially the opposite sex is 90.0% and the accuracy was 90.2%; the MCV and urinary MCV ratio of the optimal critical value is greater than or equal to 1.25 with the analysis of sensitivity of 93.5%, the specificity of 98.0%, the accuracy of 95.5% (Table 2).

Table 2. Diagnostic efficiency of different MCV and glomerular hematuria (%).

MCV Index	Sensitivity	Specificity	Accuracy
Urine MCV ≤ 70 fL	80.6	94.0	86.6
Urine MCV ≤ 75 fL	90.3	90.0	90.2
Blood MCV/Urine MCV ≥ 1.25	93.5	98.0	95.5

4. Discussion

Kidney biopsy is the gold standard for diagnosis of renal diseases. However with a certain risk, it is not easy to accept for prognosis and treatment effect need to achieve by repeated renal biopsy. Urine sample is non-invasive, and can be carry out for a continuous follow-up, besides it an important sample for early diagnosis of renal injury. At present, it is a classical method on the identification for the sources of hematuria. Unfortunately, the observation of red blood cell morphology is affected by some subjective factors, which affect the accuracy of the results. In recent years, it has been reported MCR and RDW useful in the determination of sources of red blood cells, if the distribution curve of peak value smaller than normal and MCR <72 fL, it indicate the glomerular hematuria; whether if vice versa, its non-glomerular hematuria; and if there is two peak value whereas it indicated mixed hematuria.

In recent years, there was various methods for hematuria diagnosis, but has yet to establish non-invasive, rapid and simple diagnostic method. Currently, the application of urine analyzer, hematology analyzer, and phase contrast microscopy analysis method, is used for the analysis of urinary red cell morphology and MCV [2]. It identify the presence of glomerular hematuria, which provides a new way for the diagnosis of hematuria. Difference pathogenesis of glomerulonephritis and non-glomerular hematuria, result in differences size and shape of the red blood cells presence in the urine. The possible mechanism is generally believed that, when the lesions occur within the glomerular filtration membrane, the red blood cell will diffuse from the filtration membrane into urine. The pathologic change of glomerular filtration membrane, due to mechanical extrusion after injury induce tensile strength which cause red blood cells diffuse out by high blood osmotic pressure. Hemoglobin consumption, denaturation of red blood cells in different pH values or osmotic effect of continuous change of renal tubular filtrate, cause volume of red blood cells in glomerular hematuria is much smaller than the volume of normal red blood cells. Moreover, the size of red blood cells appear shrinkage deformation and abnormal morphology changes occurred, such as oval shaped, a half-moon shaped, spike shaped, or ring shaped. Glomerular hematuria disease is mainly cause by glomeruli or following parts and urinary tract bleeding. There are absent of red blood cells in glomerular filtration membrane after injury, and the time red blood cells in tubular filtration filtrate flows through is short, hence the red blood cells didn't have or less affected, so it allow normal morphology of red blood cells in renal hematuria to maintain normal or slight uniformly changes.

In clinical practice, there are few precautions should be taken: (1) Urine samples should collected at the early morning, because the first morning sample is highly concentrated and it is conducive to improve the sensitivity of the determination. However, the first morning urine sample's bladder storage time was too long, which will affect the cell morphology, so the second morning urine sample will be better. (2) Specimens should be timely submission, red blood cells lysis occur in the sample that collected for a longer time. (3) The full automatic blood cell analyzer was designed with blood as the object, instrument has high sensitivity and accuracy when the red blood cell count in the range of $(1.00–6.00) \times 10^{12}$ cells/L. The degree

of hematuria varies with the severity of the disease, which affect the accuracy for the detection results. Hence control the number of red blood cells in the range of (1.00–6.00) $\times 10^{12}$ cells /L was done by the method of concentration and dilution for the reason when the number of red blood cells in the urine is too small, the urine MCV may not be measured or not accurate. To achieve this, patients advised collect the 3 h or 12 h of urine and embalmed. In 1 L in urine add in 400 g/L of formaldehyde for 5 mL and refrigerated. It should prevent the use of other preservative, as it will destroy the red blood cells; moreover, if there is excessive of red blood cells inside the sample, it may dilute with normal saline until the targeted range before carry out the determination.

XT-1800i MCV blood analyzer was used to directly measure urine and blood MCV, the results showed that 43 patients with glomerular hematuria MCV value was significantly less than that of peripheral blood and non-glomerular hematuria, and the rate of erythrocyte deformity was significantly higher than non-glomerular nephritis ($p < 0.01$). Because this method is simple and fast, and with high sensitivity and specificity to the renal glomerular nephritis hematuria hence it provide useful clinical application value in diagnosis of glomerular hematuria. The microscopic examination is the gold standard for diagnosis of typical of the red blood cell morphology and mixed hematuria; whereas, urinary red blood cell morphology, and MCV of urine RBC help in determine and classification of hematuria. Combination of this two detection allow to eliminate objective factors and subjective judgment error, besides that these method are fast, practical, non-invasive, able provide the differential diagnosis for different urinary system diseases, and improve the effectiveness of treatment and prognosis. As the conclusion, this paper considers that the combination of both detection of microscopic examination and blood cell analyzer provide a highly practical value in the diagnosis of glomerular hematuria.

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