

INDONESIAN JOURNAL OF  
**CLINICAL PATHOLOGY AND  
 MEDICAL LABORATORY**  
 Majalah Patologi Klinik Indonesia dan Laboratorium Medik

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## PROPORTION OF ISOMORPHIC ERYTHROCYTE URINE IN DIABETIC KIDNEY DISEASE WITH FLOW CYTOMETRY METHODS

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### ABSTRACT

Hematuria can be found in diabetic kidney disease. Urinary erythrocytes morphology can differentiate hematuria in diabetic kidney disease from other glomerular disorders. Different etiologies need different management. Urinalysis with flow cytometry method can directly give information about urine erythrocyte morphology which is not obtained by the conventional method. The aim of this study was to determine the proportion of urinary isomorphic erythrocytes in diabetic kidney disease. This was a descriptive cross-sectional study in the Dr. Hasan Sadikin Hospital Bandung from July 2016 to July 2017. Subjects were 38 patients who have been diagnosed as diabetic kidney disease by clinicians and had hematuria. Random urine samples were collected for erythrocytes morphology assay by using flow cytometry method and u-ACR values by using spectrophotometry method. The result of this study was 57.9% male, with the most frequent age were 55-64 years old group (34.2%) and 63.2% from all subject were included in the macro albuminuria category. In erythrocyte morphology assay, 84.2% was isomorphic erythrocyte which 83.3% was macro albuminuria group. The proportion of hematuria in diabetic kidney disease with automated integrated urine flow cytometry method was dominated by isomorphic erythrocyte morphology. Isomorphic erythrocytes in DM did not mean absence of glomerular abnormalities.

**Key words:** Diabetic kidney disease, flowcytometry, isomorphic erythrocytes

### INTRODUCTION

Diabetes mellitus is a metabolic disease marked with chronic hyperglycemia caused by disorders of insulin secretion, insulin activity or both.<sup>1</sup> Diabetes mellitus type 2 is the most common type of diabetes, 90% from all diabetic cases in this world. The increase in DMT2 prevalence is mostly in developing countries (69%) compared to developed countries (20%). Data from the International Diabetes Federation (IDF) in 2015 states that Indonesia is a country with the 7<sup>th</sup> most diabetic patients in the world.<sup>2,3</sup> Basic Health Research (Riskesdas 2013) report, states that the prevalence of diabetic patients in 2013 (2.1%) increased compared to 2007 (1.1%).<sup>4</sup>

Diabetic kidney disease or diabetic nephro-pathy is defined as a structural, functional and clinical disorder of the kidney caused by diabetes. Diabetic kidney disease is a microvascular complication due to DM and the most common cause of chronic kidney disease.<sup>5,6</sup>

American Diabetes Association (ADA) Consensus in 2016 and Persatuan Endokrinologi Indonesia (Perkeni) in 2015 states that the gold standard to diagnose diabetic kidney disease is the Urine Albumin to Creatinine Ratio (u-ACR).<sup>7,8</sup> Other urine parameters that can be used to diagnose diabetic

kidney disease is the urine erythrocyte morphology examination. This examination can be used to find the etiology of hematuria in diabetic kidney disease, to see whether the cause of hematuria is indeed due to diabetes or other reasons (nondiabetic).<sup>9</sup>

Hematuria can be found in patients with diabetes. The prevalence of hematuria in diabetic kidney disease is around 12.5% to 73% depending on the population and definition of hematuria used.<sup>10</sup> Hematuria in diabetic kidney disease is due to the rupture of microaneurysm in the glomerular capillary.<sup>11-13</sup>

Micro aneurysm in diabetic kidney disease is due to the enlargement of the Kimmelstiel-Wilson nodule boosted the glomerular capillary. The nodule will release erythrocytes when ruptured.<sup>14</sup> The release of erythrocytes due to the rupture of the aneurysm causes the erythrocytes automatically enter the tubules without passing the glomerular barrier, so they are not influenced by mechanical destruction and does not create a change in the shape of erythrocytes, as in other glomerular disorders, even though there is a change in erythrocyte deformability.<sup>10,14</sup>

Urine erythrocyte morphology examination with automated integrated urine flow cytometry is a

method using the automatic equipment. The interpretation of the test is done by reading the scattergram and histogram. The advantage of this method is it can save time, eliminate examination subjectivity and give direct information of erythrocytes specific shape, either isomorphic or dysmorphic.<sup>15</sup> Hematuria in diabetic nephropathy can be an indication for kidney biopsy because there is a difference in management in diabetic kidney disease and nondiabetic kidney disease. When hematuria is caused by diabetes, the patient can be given pharmacologic therapy, but if the hematuria has another etiology, the clinician must do other supporting examinations to find out the cause of hematuria.<sup>16</sup>

According to references, there is no current data about morphological description of urine erythrocytes in patients with diabetic kidney disease in Indonesia. The researcher is interested in knowing the proportion in dysmorphic and isomorphic erythrocytes, due to the importance in identifying whether the etiology of hematuria in patients with DM and previous research on erythrocytes morphology used conventional methods, hence isomorphic erythrocytes are when a group of urine erythrocytes have the same shape or are uniform. While dysmorphic erythrocytes are when urine erythrocytes morphology have different size and shapes. Urine erythrocytes with flow cytometry method are depicted in a scattergram as in Figure 1. The aim of this study was to know the proportion of isomorphic erythrocytes in patients with diabetic kidney disease using automated integrated urine flow cytometry.

## METHODS

This study was conducted from July 2016 till July 2017 and was approved by the Research Ethical Committee of the Medical Faculty of Padjajaran University.

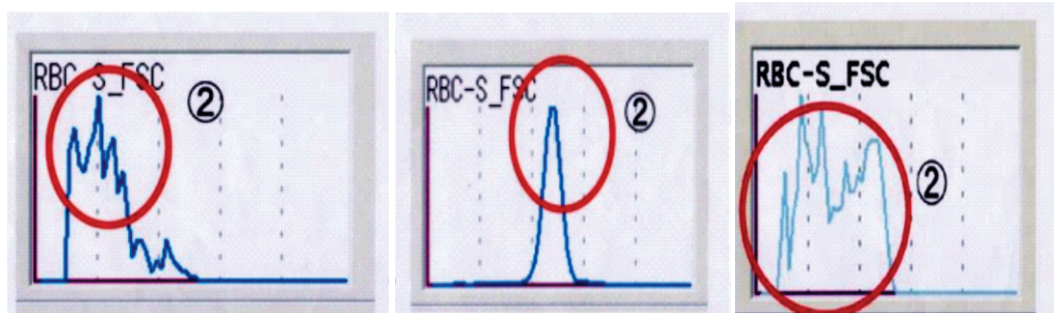
This study was observational descriptive, and the data was collected cross-sectional. The subjects of

the research were patients with diabetic kidney disease from the Outpatient Clinic and Internal Medicine Ward of the Dr. Hasan Sadikin Hospital Bandung, the clinician made diagnosis. Inclusion criteria were the patient as diagnosed with diabetic kidney disease, there was microscopic hematuria, u-ACR revealed micro or macro albuminuria, urine pH between 3-9 and SG > 1.010. The subject would be excluded if another disease caused hematuria, there was a history of consuming specific medication (anticoagulants, cimetidine, trimethoprim, corticosteroids, and cephalosporines), the patient was a female and menstruating at the time, and the time from urine being collected till examined > 2 hours.

The specimen was a random urine collection and underwent erythrocyte morphological examination using flow cytometry method (in Santo Borromeus Hospital Bandung) and u-ACR examination using spectrophotometry (Siemens Dimension EXL). Data analyzed was characteristics and clinical status of the subjects of the experiments. Data may be presented in tabulation with detailed amount or frequency and percentage.<sup>17,18</sup>

## RESULTS AND DISCUSSION

During the period of collecting subjects, 40 subjects were obtained from 148 research subjects that fulfilled inclusion and exclusion criteria and agreed to partake in this study. From 40 subjects that underwent automated integrated urine flow cytometry, there were two subjects with dysmorphic morphology urine and was conducted confirmation tests with a manual microscope due to discrepancies from blood urine from chemistry examination with urine sediments erythrocytes and there was YSL flagging that is a sign of the presence of yeast. After confirmation using a manual microscope, there was yeast in the urine sediment that was read as dysmorphic erythrocyte in the flow cytometry equipment. So these two subjects were excluded from the research data. This research only analyzed



**Figure 1.** Scattergram of urine erythrocytes using Flow cytometry a. Dysmorphic b. Isomorphic C. Mixed

38 subjects but still fulfilled the minimal amount of samples for research.

Characteristic description of the research subjects consisting of sex, age, a term of DM, compliance of therapy, type of DM therapy and uACR are stated in Table 1.

Table 1 has 57.9% male and 42.1% female subjects. The mean age is 55-64 years old range. Most of the subjects had DM < 5 years about 47.4%. From the u-ACR, there was 63.2% patient with macroalbuminuria and 36.8% with microalbuminuria.

Table 2 describes the morphology of urine erythrocytes in patients with diabetic kidney disease using flow cytometry method. There was 84.2% subject that had isomorphic erythrocyte and 15.8%

subject had mixed erythrocyte characteristics (combination of isomorphic and dysmorphic erythrocytes).

Table 3 describes the proportion of urine erythrocyte morphology with flow cytometry method in diabetic kidney disease patients with microalbuminuria and macroalbuminuria.

Table 3 divided the subjects into two groups microalbuminuria (n=14) and macroalbuminuria (n=24). In the group with microalbuminuria, there were 85.7% subjects with isomorphic erythrocyte and 14.3% with mixed erythrocyte. In the macroalbuminuria group, there was 83.3% subject with isomorphic erythrocytes and 16.7% with mixed erythrocytes.

This study found that from all subjects, 57.9%

**Table 1.** Research subjects characteristics

Variable	Amount (n =38)	Percentage (%)
<b>Sex</b>		
Male	22	57.9
Female	16	42.1
<b>Age (years old)</b>		
25-34	7	18.4
35-44	5	13.2
45-54	4	10.5
55-64	13	34.2
>65	9	23.7
<b>Term of DM (years)</b>		
<5	18	47.5
5-10	12	31.3
>10	8	21.2
<b>Compliance of therapy</b>		
Controlled	20	52.6
Uncontrolled	18	47.4
<b>u-ACR</b>	14	36.8
Microalbuminuria		
Macroalbuminuria	24	63.2
Categorical data is stated in amount/frequency and percentage		

**Table 2.** The proportion of erythrocyte urine morphology in patients with diabetic kidney disease with automated integrated urine flow cytometry

Variable	Amount (n= 38)	Percentage (%)
<b>Erythrocyte morphology</b>		
Isomorphic erythrocyte	32	84.2
Mixed erythrocyte	6	15.8
Categorical data are stated in amount/frequency and percentage		
Mixed erythrocyte: isomorphic and dysmorphic		



**Table 3.** The proportion of urine erythrocyte morphology with flow cytometry method in diabetic kidney disease patients with microalbuminuria and macroalbuminuria

Variable	u-ACR	
	Microalbuminuria (n=14) n (%)	Macroalbuminuria (n=24) n (%)
<b>Erythrocyte morphology</b>		
Isomorphic erythrocyte	12 (85.7)	20 (83.3)
Mixed erythrocyte	2 (14.3)	4 (16.7)

were males and 42.1% were females. This result was also the same as the research of Villar *et al.*<sup>19</sup> Even though the most significant percentage in this research was males; there was no considerable difference between male and female. Clotet *et al.* in 2016 stated that males with DM had the higher risk to get diabetic nephropathy compared to females. Males with diabetes had an increase in renal angiotensinogen and renin that correlates with albuminuria, increase in intraglomerular pressure and kidney fibrosis. In productive females, estrogen has a protective effect in the profibrotic and pro inflammatory process caused by hyperglycemia. In this study, from 17 female subjects, only five were in the productive age. In menopause aged female there was an increase in TGF- $\beta$ 1 expression that plays a role in tubulointerstitial inflammation and kidney fibrosis.<sup>20</sup>

This research used age groups according to Riskesdas 2013. The subjects were aged 31 – 75 years old with the largest proportion in the 55-64 years old range (34.2%). This is in accordance with Riskesdas 2013 data that states the highest prevalence of DM in Indonesia was in that age range.<sup>21</sup> Various researches showed that the incidence of Diabetes Mellitus Type 2 (DMT2) increase along with age and reaches a peak in the 6<sup>th</sup> decade. Aging is one of the DMT2 risk factors that is related to a disorder in insulin action. Aging increases insulin resistance due to a combination of several factors: obesity, mitochondrial dysfunction, hormonal changes, oxidative stress, inflammation and a decrease in physical activity. The reduction of insulin secretion by the B cell of the pancreas caused by several factors: mitochondrial dysfunction, increase in Glucose transporter 2 (GLUT2) levels, accumulation of AGEs, telomerase deficiency and a decrease in the telomere length, a decrease in  $\beta$ 2-adrenergic receptor excretion, Ca<sup>2+</sup> metabolism disorder, decreases in response towards Glucagon-like peptide1 (GLP-1) stimulation, increase in autophagy and decrease in specific beta cell gene expression.

In this study, 52.6% subjects had controlled diabetes (had a routine check-up to the doctor and had therapy as instructed) and 47.4% were uncontrolled (did not routinely went to the doctor and this was seen from medical records). Data of patients compliance was still subjective because interviews obtained it and confirmed by medical records of the patients.

Duration of DM in subjects varies between 5 to 15 years. Most of the subjects (47.5%) had DM < 5 years. According to literature, diabetic kidney disease can happen five years since DM diagnosed. These research results were different with those of Inassi *et al.* that stated that the longer someone suffers from DM, the higher one's risk of developing diabetic nephropathy.<sup>22</sup> The difference of this research's results maybe due to the data of the length of DM was obtained from interviewing the patient, and the secondary data was from medical records. Data from The National Health and Nutrition Examination Survey (NHANES) in 2012 states that from all DM patients only 58.1-79.8% were diagnosed.<sup>23</sup> Roche *et al.* stated that DM could happen 9 – 12 years before diagnosed. Delayed diagnosis may be caused by low education level, difficulty to access health facilities, an unhealthy lifestyle and not paying attention to signs and symptoms.<sup>24</sup>

This study also obtained that most of the subjects with high u-ACR were those with diabetic kidney disease with macro albuminuria (63.2%). This is suitable with Shen *et al.* states that the higher the albuminuria the higher the chances of hematuria in diabetic kidney disease. This might be due to the fact that the higher the u-ACR, the more severe the histological changes in the glomerulus.<sup>25</sup> The limitations of Shen's research is that it did not differentiate the morphology of urine erythrocytes.

Table 2 describes the proportion of urine erythrocytes in patients with diabetic nephropathy using automated integrated urine flow cytometry that resulted in 84.2% isomorphic erythrocytes and 15.8% of patients had mixed erythrocytes. This is

consistent with Gunnar's research in 2004 and Dong in 2016 that states that isomorphic erythrocytes dominated urine erythrocytes morphology in patients with diabetic kidney disease. The theory states that hematuria in diabetic nephropathy happens due to the rupture of micro aneurysm in glomerulus capillary.<sup>8,10,12</sup>

In diabetic kidney disease the erythrocytes deformability is caused by continuous hyperglycemia.<sup>10</sup> Continuous hyperglycemia for prolonged time can cause the membrane of the erythrocyte and hemoglobin to bind with glucose through glycation and an accumulation of AGEs will cause a change in rheology, causing erythrocytes to be stiff or has a lower ability to change shape compared to healthy patients. The detachment of erythrocytes due to aneurysm rupture causes the erythrocytes not to be affected by mechanical trauma causing the erythrocytes do not easily change shape, even though in patients with DM there is a change in erythrocyte deformability.<sup>9,10</sup>

This study had 15.8% subjects that had mixed erythrocyte. Late stages of diabetic kidney disease may cause the mixed type erythrocytes appearance. In the late stages of diabetic nephropathy, the damage of the glomerulus is severe, causing an increase in glomerular capillary permeability. In late stages of diabetic nephropathy, there is also a decrease in erythrocyte deformability due to hyperglycemia that causes the erythrocytes to be more rigid and easily damaged causing a dysmorphic change in the erythrocytes before micro aneurysm rupture. This condition causes a mix in dysmorphic and isomorphic erythrocyte morphology (mixed erythrocyte). This condition also needs to be assumed that there is a combination of diabetic kidney disease with other glomerulus disorders. Other glomerular diseases in patients with DM include IgA nephropathy, membranous nephropathy, focal segmental glomerulopathy, and minimal change glomerulopathy. To diagnose these damages (nondiabetic) additional examinations are needed.<sup>26</sup>

Table 3 describes the proportion of urine erythrocytes using flow cytometry in patients with diabetic kidney disease with micro albuminuria or macro albuminuria that can be seen as a percentage with a not so big difference between isomorphic erythrocytes in macro albuminuria and micro albuminuria. This research also had the description of mixed erythrocytes (isomorphic and dysmorphic) in both macro albuminuria and micro albuminuria. This showed that u-ACR levels did not influence the morphology of erythrocytes or erythrocyte

morphology didn't give a description of the severeness of albuminuria. Isomorphic urine erythrocyte description did not always show glomerular disorders in diabetic nephrotic disease.

The limitation of this research was that this research only used interview method and medical record data to show the therapy compliance. There was no data on therapy, and objective parameters such as HbA1c were not used.

## CONCLUSION AND SUGGESTION

The proportion of urine erythrocytes in diabetic nephropathy using automated integrated urine flow cytometry is mostly isomorphic. Morphological examination of urinary erythrocytes using the automated integrated urine flow cytometry method needs to be considered as a parameter to help determine hematuria in diabetic kidney disease caused by glomerular or non glomerular.

Further research still needed to find out the urinalysis validity of automated integrated flow cytometry method in diabetic kidney disease to determine the etiology of hematuria and the relationship of hematuria in DM with adherence to therapy by using more objective examination parameters, HbA1c.

## REFERENCES

1. Kharroubi AT, Darwish HM. Diabetes mellitus: The epidemic of the century. *World J Diabetes*, 2015; 6(6): 850-67.
2. Baynes HW. Classification, pathophysiology, diagnosis, and management of diabetes mellitus. *J Diabetes Metab*. 2015; 6(5): 1-9.
3. IDF diabetes atlas. Diabetes: A global emergency. International Diabetes Federation, 2015; 12-17; 7<sup>th</sup> Ed.
4. Fogo AB, Neilson EG. Atlas of urinary sediments and renal biopsies. dalam: Jameson JL, Loscalzo J, editor. *Harrison's nephrology and acid-base disorders*. Ed ke-2., USA, McGraw-Hill, 2013; 32-42.
5. Mora-Fernández C, Inguez-Pimentel VD, Fuentes MMD, Górriz J, Inez-Castelao AM, Navarro González JF. Diabetic kidney disease: From physiology to therapeutics. *The Journal of Physiology*, 2014; 592(18): 3997-4012.
6. Lim AK. Diabetic nephropathy-complications and treatment. *International Journal of Nephrology and Renovascular Disease*, 2014; 7: 361-81.
7. Dong Z-Y, Wang Y-D, Qiu Q, Hou K, Zhang L, Wu J, *et al*. Dysmorphic erythrocytes are superior to hematuria for indicating non-diabetic renal disease in type 2 diabetics. *J Diabetes Investig*, 2016; 7: 115-20.
8. Heine GH, Sester U, Girndt M, K Ohler H. Acanthocytes in the urine. Useful tool to differentiate diabetic nephropathy from glomerulonephritis *Diabetes Care*,

- 2004; 27: 190-4.
9. Brown CD, Ghali HS, Zhao Z, Thomas LL, Friedman EA. Association of reduced red blood cell deformability and diabetic nephropathy. *Kidney International*, 2005; 67: 295-300.
10. Singh M, Shin S. Changes in erythrocyte aggregation and deformability in diabetes mellitus: A brief review. *Indian Journal of Experimental Biology*, 2009; 47: 7-15.
11. 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): 63-67.
12. Alsaad K, Herzenberg A. Distinguishing diabetic nephropathy from other causes of glomerulosclerosis: An update. *J Clin Pathol*. 2007; 60: 18-26.
13. Germany. SEED-Urinalysis. Laboratory investigation of hematuria. Sysmex Corporation, 2012; 1-12.
14. Suarez MLG, Thomas DB, Barisoni L, Fornoni A. Diabetic nephropathy: Is it time yet for routine kidney biopsy. *World J Diabetes*. 2013; 4(6): 245-55.
15. Agresti A. An introduction to categorical data analysis. 2<sup>nd</sup> Ed., Hoboken, New Jersey, John Wiley and Sons, 2007; 1-20.
16. Field, A. Discovering statistics using SPSS. London, Sage Publication Ltd, 2011; 7-56.
17. Villar E, Remontet L, Labeeuw M, Ecochard R. Effect of age, gender, and diabetes on excess death in end-stage renal failure. *J Am Soc Nephrol*. 2007; 18: 2125-34.
18. Clotet S, Riera M, Pascual J, Soler MJ. Ras and sex differences in diabetic nephropathy. *Am J Physiol Renal Physiol*, 2016; F945-57.
19. Riset Kesehatan Dasar 2013. Badan penelitian dan pengembangan kesehatan. Jakarta, Kementerian Kesehatan RI, 2013; 118-125.
20. Detata V. Age-related impairment of pancreatic beta cell function: Pathophysiological and cellular mechanisms. *Front Endocrinol*. 2014; 5(138): 1-5.
21. Cerf ME. Beta-cell dysfunction and insulin resistance. *Front Endocrinol*. 2013; 4(37): 1-12.
22. Inassi JRV. Role of duration of diabetes in the development of nephropathy in type 2 diabetic patients. *National Journal of Medical Research*. 2013; 3(1): 5-8.
23. Dwyer-Lindgren L, Mackenbach JP, Lenthe FJV, Flaxman AD, Mokdad AH. Diagnosed and undiagnosed diabetes prevalence by country in the U.S. 1999-2012. *Diabetes Care*, 2016; 39: 1556-62.
24. Roche MM, Wang PP. Factors associated with a diabetes diagnosis and late diabetes diagnosis for males and females. *Journal of Clinical and Translational Endocrinology*, 2014; 1: 77-84.
25. Shen F-C, Lee C-T, Sun C-K, Chung M-S, Lee J-J, Chang H-W, *et al*. Prevalence of hematuria positively associated with urine albumin excretion in type 2 diabetes. *Diabet Med*. 2012; 29: 1178-83.
26. Zhuo L, Zou G, Li W, Lu J, Ren W. Prevalence of diabetic nephropathy complicating non-diabetic renal disease among Chinese patients with type 2 diabetes mellitus. *Eur J Med Res*. 2013; 18(1): 4-9.