IJRETINA
International Journal of Retina

URINE ALBUMIN CREATININE RATIO AMONG DIABETIC RETINOPATHY PATIENT WITH AND WITHOUT DIABETIC MACULAR EDEMA IN MOH. HOESIN HOSPITAL PALEMBANG

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ABSTRACT

Introduction: Diabetic Macular Edema is a diffuse thickening in macula which can be found in various severity of Diabetic Retinopathy. There are issue about relationship between Diabetic Macular Edema and albuminuria caused by chronic renal failure. The aim of this study is to know and compare urine albumin creatinine ratio among Diabetic Retinopathy patients with and without Diabetic Macular Edema in Moh. Hoesin Hospital.

Methods: Cross sectional study with 25 sample was conducted. Diabetic Retinopathy and Diabetic Macular Edema was classified base on Early Treatment Of Diabetic Retinopathy Study (ETDRS) criteria. T-test, odd ratio and multiple logistic regretion analysis was used to analysed sociodemography characteristic (age and gender), clinical characteristic (duration of DM, hipertension, treatment, body mass indeks and antioksidan consumption), ophtalmology characteristic (visus, anterior segment anomaly and posterior segment/ severity of Diabetic Retinopathy), laboratory characteristic (HbA1c, ureum, creatinine, urine albumin creatinine ratio, and lipid profile).

Result: Urine albumin creatinine ratio mean (2146.77 ± 3796.19) in Diabetic Macular Edema and (49.0 ± 45.35) in non-Diabetic Macular Edema; cutoff point 62.00 mg/dL. Odd ratio adjusted for urine albumin creatinine ratio = 18,8. In this research, risk factors which has significantly were urine albumin creatinine ratio (p=0.047) and High-Density Lipoprotein/HDL (p=0.028) with odd ratio 8.571 and 6.67 respectively. Urine albumin creatinine ratio showed significantly high Mann whitney analysis 0.02 (p<0.005).

Conclusion: Urine albumin creatinine ratio in Diabetic Retinopathy with Diabetic Macular Edema was higher than without Diabetic Macular Edema. Urine albumin creatinine ratio and High Density Lipoprotein (HDL) are the two important risk factors associated with Diabetic Macular Edema.

INTRODUCTION

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Diabetic retinopathy is a chronic progressive the leading cause of new blindness in adults 20- 70 years of age caused by long hiperglicemic status. Among Diabetic retinopathy patients, Diabetic Macular edema can be found. Diabetic Macular Edema is a diffuse or focal thickening in macula. In addition to visual loss, the negative impact of Diabetic Macular Edema especially on patients health-related quality of life (QoL). Base on Banu Turgut Ozturk, patient with Diabetic Macular Edema consume significantly more healthcare resources, incur higher costs, and have low work efficiency compared to diabetic patients without retinal complications.[1-6]

Diabetic Macular Edema can accompany every stage of Diabetic Retinopathy. The incidence is 3% for mild non proliferative Diabetic Retinopathy, 38% for moderate and severe non proliferative Diabetic Retinopathy,

and 71% for proliferative Diabetic Retinopathy. About one diabetic patient in four can be expected to develop Diabetic Macular Edema in a lifetime. Once a patient's medical management has been optimize, ocular therapies should beconsidered to prevent progression vision loss and optimize the patient's vision.[1,2,7]

The major microvascular complications, retinopathy and nephropathy are the more important causes of blindness and end-stage renal disease. Chronic Kidney Disease and Diabetic Retinopathy are reflected in the clinical manifestations of similar microvascular lesions in the glomerular and retinal vessels.[3,7]

Many study found relationship between urine albumin creatinine ratio with diabetic retinopthy. High urine albumin creatinine ratio shows endothelial disfungtion and may influence microvasculature of the kidney and retina. Previous studies have shown that urine albumin creatinine rasio not only is important clinical marker for chonic kidney disease but also is closely associated to progression of diabetic retinopathy.[8-12]

The aim of this research is to know and compare urine albumin creatinine ratio among Diabetic Retinopathy patients with and without Diabetic Macular Edema in Moh. Hoesin Hospital.

METHODS

Cross sectional study with 25 subject diabetic retinopathy was conducted in polyclinic/ward ophthalmology and internist of RSUP Moh. Hoesin Palembang on October 2016 until October 2017. Inclusion critteria : subject was diagnosed diabetic retinopathy with and without diabetic macular edema and willing to follow this research. Exclusion criteria : high intraocular pressure, infection in eye and infection urinary tract or nephrolithiasis/uretrolithiasis. Diabetic Retinopathy and Diabetic Macular Edema was classified base on Early Treatment Of Diabetic Retinopathy Study (ETDRS) criteria. Subject was interviewed and examined (body mass, height, blood pressure, ophthalmology and blood/urine withdrawal).

RESULT

In interim analysis with 25 subject, urine albumin creatinine rasio was significantly higher in patient diabetic retinopathy with diabetic macular edema just than without diabetic macular edema. So the research can be terminated. Risk factor of Diabetic macular edema was divided in many characteristic : sociodemography characteristic (age and gender), clinical characteristic (duration of DM, hipertension, treatment, body mass indeks and antioksidan consumption), ophtalmology characteristic (visus, anterior segment anomaly and posterior segment/ severity of Diabetic Retinopathy), laboratory characteristic (HbA1c, ureum, creatinine, urine albumin creatinine ratio, and lipid profile). There were no significantly between diabetic macular edema and sociodemography characteristic.

Table 1. **Sociodemography Characteristic**

Sociodemography	N	%	Average
Age			
<40 year	1	4	
40-49 year	8	32	
50-59 year	10	40	53.80 ± 8.25
≥60 year	6	24	
Total	25	100	
Gender			
Male	10	40	
Female	15	60	
Total	25	100	
Occupation			
Enterpreneur	10	40.0	
Civil servant	5	20.0	
Jobless	9	36.0	
Pension	1	4.0	
Total	25	100	
Education			
Elementary school	6	24.0	
Secondary school	5	20.0	

Senior high school		3		12.0
Collage		11		44.0
	Total	25		100

In this research, there were 13 subject with diabetic macular edema and 12 without diabetic macular edema. There were no significantly between diabetic macular edema and clinical characteristic.

Table 2. **Clinical Characteristic**

Clinical	DME Positive		DME Negative		Total	P
	N	%	N	%		
Hipertenssion Complication						
Yes	6	60	4	40	10	*0,513
No	7	46,67	8	53.3	15	
Treatment						
OHO	4	36.4	7	63.6	11	*0,165
Injection	9	64.3	5	35.7	14	
BMI						
Underweight	0	0	0	0	0	*0,552
Normoweight	5	62.5	3	37.5	8	
Overweight	3	50.0	3	50.0	6	
Obesity	5	45.5	6	54.5	11	
Antioxidant Consumption						
Yes	9	50	9	50	18	*0,748
No	4	57,1	3	42,9	**7**	

In this research, risk factors which has significant odd ratio were urine albumin creatinine ratio and High Density Lipoprotein (HDL) 8.571 and 6.67 respectively. Urine albumin creatinine ratio showed significantly high Mann whitney analysis 0.02 (p<0.005). But, there were no relationship between ophthalmology characteristic and in laboratory characteristic, only urine albumin creatinine ratio (p=0,047) and High Density lipoprotein/HDL (p=0,028) were significantly with odd ratio 8.571 and 6.67.

Table 3. **Laboratory Characteristic**

Laboratory Characteristic	DME Positive		DME Negative			p	OR
	N	%	N	%			
HbA1C							
Increased	11	61.1	7	38.9	18		
Normal	2	28.6	5	71.4	7	0.144	
Kreatinin							
Increased /Critical	9	60.0	6	40.0	15		
Normal	4	40.0	6	60.0	10	0.284	
Ureum							
Increased	7	77.8	2	22.2	9		
Normal	6	37.5	10	62.5	16	0.063[+]	

Urine Albumin Creatinine Ratio							
Increased	12	63,2	7	36,8	19		8,57
Normal	1	16,7	5	83,3	6	0.047	
Total Lipid							
Increased	9	64,3	5	35,7	14		
Normal	4	36,4	7	63,6	11	0.165	
LDL							
Increased	10	50	10	50	20		
Normal	3	60	2	40	5	*1.00	
Trigliseride							
Increased	9	69,2	4	30,8	13		
Normal	4	33,3	8	66,7	12	*0.073	
HDL							
Decreased	10	71,4	4	28,6	14		6,67
Normal	3	27,3	8	72,7	11	0.028	
Dislipidemia							
Yes	13	54,2	11	45,8	24	0.480	
No	0	0,0	1	100	1		

Differentiation between Urine Albumin Creatinine Ratio among Diabetic Retinopathy Patients with and without Diabetic Macular Edema

Base on normality test, the data of diabetic macular edema on urine albumin creatinine ratio distribution were abnormal so writer use independent sampels Mann whitney test.

Table 4. **Differentiation Urine Albumin Creatinine Rasio among Diabetic Retinopathy with and Without Diabetic Macular Edema**

	Mean ± SD	Median (Min – Max)	p*
Positive DME	2146.77 ± 3796.19	356 (38 – 13628)	0.002
Negative DME	49.0 ± 45.35	38.5 (5 – 169)	

* Mann-Whitney test

Urine albumin creatinine ratio mean (2146.77 ± 3796.19) in Diabetic Macular Edema and (49.0 ± 45.35) in non Diabetic Macular Edema; independent sampels Mann whitney test highly significant (p=0,02); cutoff point 62.00 mg/dL. Sensitivity 76.9% and specificity 75.0%, predictive positif value 76.9%, predictive negaitif value 75.0%. Odd ratio adjusted for urine albumin creatinine ratio = 18,8.

Multivariat analytic show signifantly among diabetic macular edema with urine albumin creatinine and High Density lipoprotein. The formula :

$Y_{(Diabetic\ Macular\ Edema)}$ =-0.696 + 2.934 urine albumin creatinine– 0,64 HDL.

Explanation :
- Urine albumin creatinine ratio :
    - 0 if the value under 62 mg/dL
    - 1 if the value above62 mg/dL
- High Density Lipoprotein in mg/dL
- *Odd ratio adjusted* urine albumin creatinine ratio = 18,8, means patient diabetic retinopathy with urine albumin creatinine ratio > 62 mg/dL has probability dibetic macular edema 18,8 times than they are with urine albumin creatinine ratio < 62 mg/dL.

DISCUSSION

Many research had been done to connect diabetic macular edema and chronic kidney disease. According to Kang et al., in patients with serous-type diabetic macular edema, albumin and other body fluids leak into the subretinal space through an external limiting membrane because of destruction of the inner blood retinal barrier. Nam Kyun Koo results show a significantly higher frequency of serous-type macular edema in patients with albuminuria. Despite a lack of statistical significance, serous-type macular edema usually occurred in patients with a lower level of serum albumin. These results indicate that serous-type macular edema might have a relationship with the excretion of albumin into the urine due to decreased renal function. It is also presumed that the excretion of albumin and the decreased concentration

of serum albumin cause an overload of body fluids and decreased intravascular osmotic pressure, which leads to the occurrence of serous- type macular edema.[13]

Akihiro Ishibawa et al (2013) about relationship among diabetic macular edema and chronic kidney disease in patients with type 2 diabetes shows serous retinal detachment developed 28,2% of the chronic kidney disease (-) group and 63,6% of the chronic kidney disease (+) group, a difference that reached significance (p=0.015).[14]

Gagan Sathya Prakash (2016) did research which related to Clinically Significant Macular Edema (CSME) in Diabetes Melitus type 2. In this sudy, the incidence of microalbuminuria is significantly associated with CSME. 81,2% patients with CSME had macroalbuminuria and 12,9% patients with CSME had microalbuminuria.[15]

Ong ming Jew et al (2012) the urea and cretinine level were significantly higher in the CSME grup. The urea level in the CSME and non-CSME (6.530±3.171)mmol/L and (5.078±1.747) mmol/L. Whereas the creatinine level were (125.00±86.02)mmol/L and (90.94±36.76) mmol/L respectively. The albumin level in the CSME and non-CSME were (40.24±4.47) mmol/L and (44.12±2.32) mmol/L respsctively.[16]

In this research, urine albumin creatinine level higher in diabetic retinopathy with diabetic macular edema than without diabetic macular edema. And it is showed chronic kidney disease significantly higher with diabetic macular edema. Hypoalbumin, caused by renal leakage. Hypoalbumin effect osmotic pressure (decrease) in plasma and this factor cause macular edema. Decrease osmotic pressure cause the liquid extravasasion leave the vascular to fill around tissue.

Many studies had been done to identify the risk factors or association of diabetic macular edema. However, the association varied from one study to another. The variaton in the result may be due among other things to epidemiological differences. In this research, urine albumin creatinine and High Density Lipoprotein/HDL significantly high with diabetic macular edema.

In this research, there were limitation : we didn't do Optical Coherence Tomographi (OCT) to know macular thickness kuantitatively and albumin serum to know hypoalbuminemia which caused edema generalisation. Besides, only 25 subject participated so we suggested to add the research subject.

CONCLUSION

Urine albumin creatinine ratio in Diabetic Retinopathy with Diabetic Macular Edema was higher than without Diabetic Macular Edema. Urine albumin creatinine ratio and High Density Lipoprotein (HDL) are the two important risk factors associated with Diabetic Macular Edema.

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