

ASSESSMENT OF ALBUMIN GLOBULIN RATIO IN TYPE 2 DIABETIC PATIENTS WITH NON ALCOHOLIC FATTY LIVER DISEASE

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a common chronic disease, and its incidence has increased at an alarming rate in recent years. According to the International Diabetes Federation, the global prevalence of T2DM is expected to rise to affect one-tenth of the population by the next decade. Therefore, this study aimed to systematically explore the association of globulin and AGR with DKD. **Materials and Methods:** A cross-sectional study was done among the patients attending a tertiary care hospital of Bihar during the February 2024 to January 2025. A total of 200 participants completed the interview in this cycle. DM was diagnosed by both laboratory tests and questionnaires, with fasting plasma glucose ≥ 126 mg/dL, glycated hemoglobin (HbA1c) $\geq 6.5\%$, or 2-hours oral glucose tolerance test (OGTT) ≥ 200 mg/dL as the laboratory diagnostic criterion based on the American Diabetes Association. **Result:** A total of 200 T2DM patients were included in this study. The median age of the study participants was 59.8 years with majority of them in their 7th or 8th decade of life. Around one-third of the patients had DKD. Compared with patients without DKD, those with DKD had higher levels of globulin and lower levels of AGR. For other baseline characteristics, both had older age, longer duration of diabetes, a higher proportion of insulin use, a higher proportion of hypertension, higher BMI, higher levels of FPG, HbA1c, and urinary albumin. **Conclusion:** In our study, patients with a higher AGR had higher albumin levels and lower globulin levels. Therefore, a higher AGR may be caused by high levels of albumin, low levels of globulin, or a combination of both.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a common chronic disease, and its incidence has increased at an alarming rate in recent years. According to the International Diabetes Federation, the global prevalence of T2DM is expected to rise to affect one-tenth of the population by the next decade.^[1] Among them, China has the largest number of T2DM patients, contributing to one-quarter of the global patients of this disease. The threat of T2DM to human health mainly comes from chronic complications, among which diabetic kidney disease (DKD) and diabetic retinopathy (DR) are the most common microvascular complications of T2DM. The occurrence of DKD and DR are closely related, and many studies have shown that DKD and DR can predict each other.^[2-4] About 30–40% of T2DM patients have DKD,^[5] and nearly 50% of them will eventually develop end-stage kidney disease,^[6] shortening the life span of T2DM patients. About

one-third of T2DM patients will have DR, which can rapidly progress to vision-threatening DR if not treated promptly, resulting in irreversible vision impairment.^[7] DKD affect the quality of life of T2DM patients and also bring heavy medical burdens to patients and society. Therefore, it is necessary to comprehensively study the risk factors of DKD. Studies have shown that controlling blood glucose alone cannot prevent the development of chronic microvascular complications of T2DM,^[8] so attention has focused on the relationship between other risk factors such as inflammation and chronic microvascular complications.

Inflammation plays a crucial role in the occurrence and progression of DKD.^[9] Serum albumin and globulin are biomarkers of systemic inflammation, and the relationship between lower levels of serum albumin and increased risk of DKD,^[10-15] but this is not the case for serum globulin. Globulin is synthesized and secreted by liver and plasma cells in response to inflammation and infection. Globulin is

the main component of non-albumin in serum and is composed of a variety of proinflammatory proteins including immunoglobulin and acute phase proteins.^[16] Elevated serum globulin concentrations are the result of the accumulation of immunoglobulin's and acute inflammatory proteins, and these changes are key markers of the degree and severity of inflammation and immune.^[17] Therefore, this study aimed to systematically explore the association of globulin and AGR with DKD.

MATERIALS AND METHODS

A cross-sectional study was done among the patients attending a tertiary care hospital of Bihar during the February 2024 to January 2025. A total of 200 participants completed the interview in this cycle. DM was diagnosed by both laboratory tests and questionnaires, with fasting plasma glucose ≥ 126 mg/dL, glycated hemoglobin (HbA1c) $\geq 6.5\%$, or 2-hours oral glucose tolerance test (OGTT) ≥ 200 mg/dL as the laboratory diagnostic criterion based on the American Diabetes Association. DM was identified if any of the above conditions were met. All detailed processes of data acquisition are obtained online such as laboratory methodology, data processing, and editing, laboratory quality assurance and monitoring, analytic notes, etc. Serum globulin was the primary independent variable focused on in this study from the standard biochemistry profile and the corresponding missing data were excluded. The following categorical or continuous variables below were considered as covariates: age, sex, race, marital status, education, alcohol, smoking, BMI, waistline, weight, albumin, hemoglobin, blood pressure, and total physical activity. Participants who were married and living with a partner were defined as married, others as unmarried. Education is categorized as below high school, high school, and above high school. Alcohol status is defined as having had at least 12 drinks per lifetime.

Both current and former smokers were defined as having smoked 100 cigarettes in their lifetime, with current smokers being defined as those who answered "every day" and "some days" to the question "Do you smoke cigarettes now," former smokers otherwise, and never smokers as those who had not smoked 100 cigarettes in their lifetime. Readings were taken for 3 consecutive blood pressure (BP) measurements and takes the mean of the BP used as an indicator for this study, high BP was defined as systolic pressure ≥ 140 mm Hg and/or diastolic pressure ≥ 90 mm Hg. Total activity is defined as the sum of all work and recreational activities during the week, that is, the sum of activity days multiplied by the time in a week, using the equation: days of vigorous work \times minutes of vigorous-intensity work + days of moderate work \times minutes of moderate-intensity work + days of walking or cycling \times minutes of walking or cycling for transport + days of vigorous recreational activities \times minutes of vigorous recreational activities + days of moderate recreational activities \times minutes of moderate recreational activities.

RESULTS

A total of 200 T2DM patients were included in this study. The median age of the study participants was 59.8 years with majority of them in their 7th or 8th decade of life. Around one-third of the patients had DKD. Compared with patients without DKD, those with DKD had higher levels of globulin and lower levels of AGR. For other baseline characteristics, both had older age, longer duration of diabetes, a higher proportion of insulin use, a higher proportion of hypertension, higher BMI, higher levels of FPG, HbA1c, and urinary albumin. They both had lower levels of education, urinary creatinine, and eGFR as compared with those without DKD. [Table 1] The characteristics of participants according to the tertiles of globulin and AGR have been shown in [Table 2].

Table 1: Characteristics of the Study Participants

Baseline characteristic	DKD		P value
	Positive (64/200)	Negative (136/200)	
Age (years)			
<60 years	37(57.8%)	101(74.3%)	<0.05
≥ 60 years	27(42.2%)	35(25.7%)	
Sex			
Male	33 (51.6%)	71 (52.2%)	>0.05
Female	31 (48.4%)	65 (47.8%)	
Area			
Urban	30 (46.9%)	74 (54.4%)	>0.05
Rural	34 (53.1%)	62 (45.6%)	
Educational level			
Primary or below	21 (32.8%)	42 (30.9%)	<0.05
Middle	19 (20.3%)	48 (35.3%)	
High school or above	24 (37.5%)	46 (33.8%)	
Current smoker	16 (25.0%)	31 (22.8%)	>0.05
Current drinker	18 (28.1%)	39 (28.7%)	>0.05
Family history of DM	29 (45.3%)	15 (11.1%)	<0.05
BMI (kg/m ²)	26.7	23.6	<0.05
Hypertension (mm/Hg)	51 (79.9%)	65 (47.8%)	<0.05
FPG (mmol/l)	8.63	6.89	<0.05
HbA1c (%)	8.1	6.2	<0.05
Urine albumin (mg/l)	49.1	49.2	>0.05
Urine globulin (mg/l)	29.9	28.7	<0.05
AGR	1.7	1.6	<0.05

Table 2: Association of Globulin and AGR with DKD in the Logistic Regression Models

Parameter	Event (%)	OR (95% CI)
Globulin (continuous)	175	1.08 (1.05, 1.11)
AGR (continuous)	175	0.35 (0.28, 0.72)

DISCUSSION

This study comprehensively analyzed the association of serum globulin and AGR with DKD in T2DM patients. We found there was a relationship between globulin and DKD, as well as between AGR and DKD. These results suggest that DKD screening should be performed in T2DM patients with high globulin and low AGR levels, especially in men. Globulin levels are closely related to immune and inflammatory states, and studies have shown that globulin is positively correlated with the severity of chronic inflammation.^[18] A previous cohort study of the Pima Indian population found that high levels of globulin were associated with T2DM,^[19] confirming the role of globulin in the development of T2DM. In the past, one study analyzed the association between serum globulin and DKD risk in 4393 diabetes people in the United States, and found that high levels of globulin increased the risk of DKD.^[13] Our study found that a higher AGR level was a protective factor for DKD. Previous studies have also reported a negative correlation between AGR and chronic inflammation.^[20] For example, studies in non-chronic kidney disease populations have found that low AGR was an independent predictor of the development of chronic kidney disease and had a stronger predictive value than other inflammatory markers such as white blood cell count and high-sensitivity C-reactive protein. Under inflammatory and infectious conditions, there is an inverse relationship between albumin and globulin, resulting in a decrease in AGR.^[21] In our study, patients with a higher AGR had higher albumin levels and lower globulin levels. Therefore, a higher AGR may be caused by high levels of albumin, low levels of globulin, or a combination of both. The positive association between serum globulin levels and DKD has been explained in the previous section. As for albumin, it has been reported to be negatively regulated by the acute phase reactants and is considered a biomarker of inflammation and nutritional status,^[22] and it decreases after inflammatory stimulation.^[23] Albumin is synthesized and secreted by liver cells and is the most abundant protein in peripheral plasma.

CONCLUSION

In our study, patients with a higher AGR had higher albumin levels and lower globulin levels. Therefore, a higher AGR may be caused by high levels of albumin, low levels of globulin, or a combination of both. The positive association between serum globulin levels and DKD has been explained in the

previous section. As for albumin, it has been reported to be negatively regulated by the acute phase reactants and is considered a biomarker of inflammation and nutritional status, and it decreases after inflammatory stimulation. Albumin is synthesized and secreted by liver cells and is the most abundant protein in peripheral plasma.

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