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Glycated Albumin Versus HbA1c in the Evaluation of Glycemic Control in Diabetic Patients With CKD

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Introduction: It is inaccurate to assess blood glucose with glycated hemoglobin (HbA1c) in patients with diabetes and chronic kidney disease (CKD), and whether glycated albumin (GA) is better than HbA1c in these patients remains unclear.

Methods: We searched PubMed, Embase, Web of Science, Scopus, the Cochrane Library, and MEDLINE to July 2017 for studies that investigated the correlation between GA or HbA1c and the average glucose levels (AG) relevant to this theme. Statistical analysis was performed using RevMan5.3 and Stata12.0. The outcome was the correlation coefficient between GA or HbA1c and AG. For the first time, we made a comparison of GA and HbA1c in different CKD stages.

Results: A total of 24 studies with 3928 patients were included. Early stages of CKD refer to CKD stage 1 to 3. Advanced CKD refer to CKD stage 4 and 5 including patients receiving dialysis. The meta-analysis suggested that in early stages of CKD, the pooled R between GA and AG was 0.61 (95% CI = 0.49−0.73) and 0.71 (95% CI = 0.55−0.87) for HbA1c ($P > 0.05$). In advanced CKD patients, the pooled R between GA and AG was 0.57 (95% CI = 0.52−0.62), and 0.49 (95% CI = 0.45−0.52) for HbA1c ($P = 0.0001$).

Conclusion: GA is superior to HbA1c in assessing blood glucose control in diabetes patients with advanced CKD.

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KEYWORDS: chronic kidney disease; diabetes mellitus; glycated albumin; HbA1c
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UNCORRECTED PROOF

Chronic kidney disease (CKD) is a worldwide public health problem that affects millions of people of all racial and ethnic groups. Diabetes mellitus is a leading cause of CKD, and it is also an important comorbidity in established CKD.[1] The rapidly increasing prevalence of diabetes worldwide virtually ensures that the proportion of CKD attributable to diabetes will continue to rise.[2,3] Glycemic control may decrease the incidence of new-onset microalbuminuria,[4] delay the progression of diabetic nephropathy,[5] limit end-organ damage, and reduce cardiovascular morbidity and mortality in uremic patients on hemodialysis.[6] Compared to the general population, glycemic control in patients with CKD is complicated by alterations in glucose and insulin homeostasis.[7] Therefore, choosing reliable clinical biomarkers to monitor glycemic control is critical in patients with both diabetes and CKD.

Glycated hemoglobin (HbA1c), glycated albumin (GA), fructosamine, and 1,5-anhydroglucitol (1,5-AG) are biomarkers used for evaluating glycemic control. At present, HbA1c, which reflects average glucose levels (AG) over the 120 days preceding the test, is widely used as a gold standard index for glycemic control in clinical practice. However, the HbA1c levels may be erroneous in patients with CKD[8] because of factors such as anemia (due to reduced erythrocyte life span or iron deficiency), and the administration of erythropoietin.[9,10] 1,5-AG reflects the degree of excretion of urinary glucose and is influenced by foods ingestion and by threshold of glucose in the kidney. Fructosamine is a generic term that refers to all glycated serum proteins including GA in blood serum. It has a shorter half-life than HbA1c, as it reflects 1 to 3 weeks of glycemic status. However, fructosamine depends not only on glucose concentrations but also on the concentration of individual plasma proteins, and these may vary greatly in CKD.[11]

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GA measures specifically the glycation product of albumin; it has been developed as an index for glycemic control,[12] but it is not affected by serum albumin levels because its ratio to total serum albumin is calculated.[13] To date, serum GA has been suggested as a more reliable and sensitive glycemic index to replace HbA1c in diabetic patients with CKD,[14–17] because it is not influenced by anemia and associated treatments. In addition, GA may also reflect the status of blood glucose more rapidly than HbA1c, and it is beneficial to patients with wide variations in blood glucose or those at higher risk for hypoglycemia.[7] However, these benefits have not been verified by large-scale clinical trials and systemic meta-analyses. Therefore, it is necessary to perform a meta-analysis to address these issues.

METHODS

Search Strategy

On 31 July 2017, we searched PubMed, Embase, Web of Science, Scopus, the Cochrane Library, and MEDLINE databases for articles about GA or HbA1c as an index of glycemic control in diabetic patients with CKD. The predefined searching key words were [“Glycated albumin” OR “Glycated hemoglobin”] AND “Kidney”, [“Glycated albumin” OR “Glycated hemoglobin”] AND “Renal”, [“Glycated albumin” OR “Glycated hemoglobin”] AND “Dialysis” through keywords searching systems. The search was limited to publications written in English to match our translation capacity.

Selection Criteria

Inclusion criteria were as follows: original and observational research; investigation of the relationship between the GA or HbA1c and AG levels; participation of diabetic patients with CKD; inclusion of the correlation coefficient and the number of patients; and full manuscript publication.

Exclusion Criteria

Exclusion criteria were as follows: animals used as research subjects; systematic review or meta-analysis; studies without the correlation coefficient and the number of patients; and articles not written in English.

Quality Assessment and Data Extraction

Data were extracted independently according to the above-mentioned selection and exclusion criteria; selection process details are shown in the Figure 1. The information extracted from each publication, in the form of a table, included the following: authors, year of publication, nation of origin, number and mean age of patients, patients’ CKD status, Pearson or Spearman

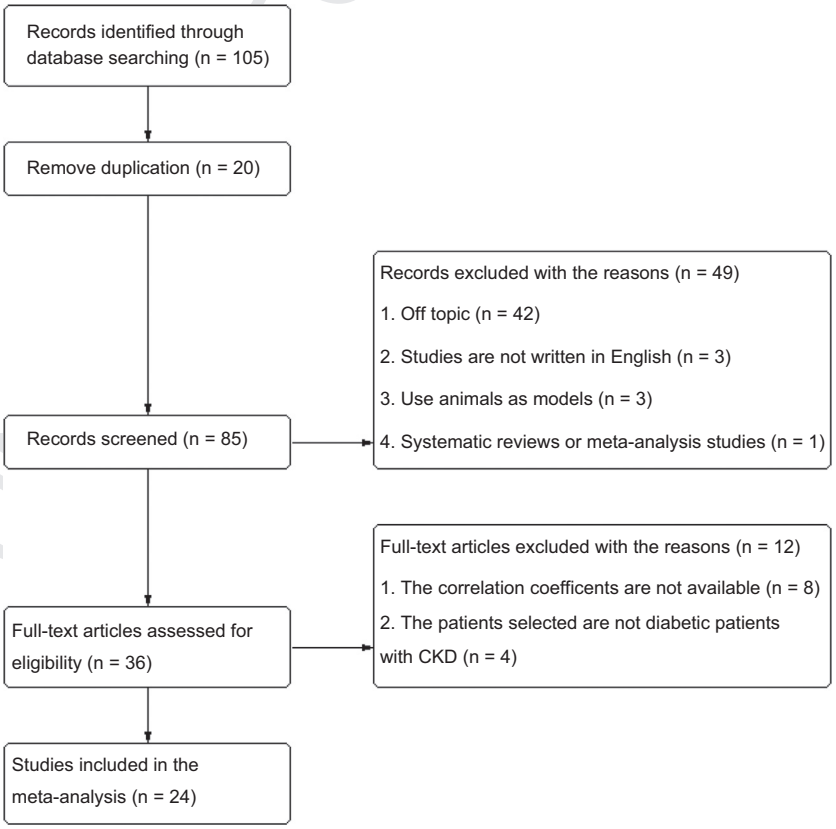

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of identification process for eligible articles. CKD, chronic kidney disease.

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