Investigating the Prognostic Value of Serum Albumin Levels in Patients Undergoing Hemodialysis: A Systematic Review and Meta-analysis

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Abstract

Background: Hypoalbuminemia, characterized by low serum albumin levels, is frequently observed in patients undergoing hemodialysis and has been identified as a potential predictor of increased mortality risk. This systematic review aims to evaluate the relationship between hypoalbuminemia and mortality in hemodialysis patients, assessing the prognostic value of serum albumin levels as an indicator for patient outcomes.

Methods: A comprehensive search was conducted in databases including PubMed, Europe PMC, and Scopus to identify relevant studies. Studies were included if they investigated the association between serum albumin levels and mortality outcomes in adult patients undergoing hemodialysis. Data extraction was performed independently by two reviewers, focusing on study characteristics, patient demographics, albumin levels, and mortality outcomes. Quality assessment of studies was conducted using the Newcastle-Ottawa Scale (NOS).

Result: A total of eight studies, encompassing 45,178 hemodialysis patients with a mean age in the 50s, met the inclusion criteria. The studies had a combined male cohort of 22,501 individuals. The definition of hypoalbuminemia varied across studies, with cutoff values ranging from 3.0 to 3.9 g/dL. Follow-up durations spanned from as early as 3 months to a maximum of 6.1 years. The meta-analysis revealed a pooled hazard ratio (HR) of 1.08 (95% CI: 0.94–1.25), suggesting a non-significant association between hypoalbuminemia and increased mortality risk (P = 0.28). However, substantial heterogeneity was present (I^2 = 79%), indicating variability across studies.

Conclusions: Hypoalbuminemia showed a non-significant association with mortality in hemodialysis patients, though variability across studies suggests further research is needed for clarity.

Introduction

Patients with end-stage renal disease (ESRD) undergoing maintenance hemodialysis face a markedly increased risk of morbidity and mortality, primarily due to cardiovascular complications, malnutrition, and inflammation.[1,2] Among various biochemical markers, serum albumin has emerged as a key indicator of nutritional and inflammatory status. Low serum albumin levels, or hypoalbuminemia, are frequently encountered in hemodialysis populations and have been consistently associated with adverse clinical outcomes, including hospitalization, infection, and mortality.[3,4]

From a clinical perspective, serum albumin measurement is routinely performed in dialysis units due to its simplicity, cost-effectiveness, and availability, making it a practical biomarker for risk assessment.[5–7] However, while hypoalbuminemia is recognized as a marker of poor prognosis, its precise prognostic value remains incompletely defined.[8,9] Understanding this relationship is crucial for guiding interventions aimed at improving survival in hemodialysis patients.

Given the high burden of mortality in this patient group and the widespread use of serum albumin as a monitoring tool, a systematic evaluation of existing evidence is warranted to clarify its prognostic significance. Therefore, this study aims to investigate the prognostic value of serum albumin levels in patients undergoing hemodialysis through a systematic review and meta-analysis.

Material And Methods

Please state the study design and its methodology. Details relevant to the conduct of the study

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines.[10]

A comprehensive electronic search was performed across PubMed, Europe PMC, and Scopus databases from inception until October 18, 2025, to identify studies investigating the association between serum albumin levels and mortality among adult patients undergoing maintenance hemodialysis. Search terms combined Medical Subject Headings (MeSH) and free-text words related to “albumin,” “hemodialysis,” and “mortality.” Detailed search terms is presented in table 1. Reference lists of eligible studies and relevant reviews were also screened to ensure completeness of the evidence base.

Table 1. Search strategy used in each database

Database	Search queries used
PubMed	("hypoalbuminaemia"[All Fields] OR "hypoalbuminemia"[MeSH Terms] OR "hypoalbuminemia"[All Fields]) AND ("renal replacement therapy"[MeSH Terms] OR

	("renal"[All Fields] AND "replacement"[All Fields] AND "therapy"[All Fields]) OR "renal replacement therapy"[All Fields] OR ("haemodialysis"[All Fields] OR "renal dialysis"[MeSH Terms] OR ("renal"[All Fields] AND "dialysis"[All Fields]) OR "renal dialysis"[All Fields] OR "hemodialysis"[All Fields])) AND ("mortality"[MeSH Terms] OR "mortality"[All Fields] OR "mortalities"[All Fields] OR "mortality"[MeSH Subheading])
Scopus	hypoalbuminemia AND renal AND replacement AND therapy OR hemodialysis AND mortality
Europe PMC	hypoalbuminemia AND renal replacement therapy OR hemodialysis AND mortality

Studies were eligible for inclusion if they were original observational investigations, either prospective or retrospective in design, that evaluated the relationship between serum albumin levels and mortality in adult patients (≥18 years) undergoing regular hemodialysis. Studies were excluded if they involved pediatric populations, patients treated with peritoneal dialysis, case reports, reviews, conference abstracts, or editorials lacking primary data. Articles were also excluded if mortality outcomes were not reported or if data were insufficient to compute risk estimates.

The primary outcome of interest was all-cause mortality among adults undergoing maintenance hemodialysis. Mortality was defined as death from any cause during the follow-up period, as reported in each study. When available, cause-specific mortality and both adjusted and unadjusted risk estimates were extracted for descriptive and comparative analyses. Studies reporting survival outcomes without explicitly defining mortality were included if sufficient data could be extracted to compute relative risk estimates.

All retrieved titles and abstracts were independently screened by two reviewers who were blinded to each other's decisions, and full texts of potentially eligible studies were then assessed for final inclusion. Disagreements regarding study eligibility were resolved through discussion and consensus. Following data saturation of included studies, a manual hand-search of their reference lists was performed to identify additional relevant records.

Data extraction was conducted independently by the same two reviewers using a pre-designed data collection form. Extracted information included study characteristics (author, year, country, and design), sample size, demographic and clinical data of participants, serum albumin measurement methods and thresholds, follow-up duration, and reported mortality outcomes. Extracted effect measures were recorded as hazard ratio (HR) or equivalent estimates with their corresponding 95% confidence intervals (CIs). Any discrepancies in data extraction were

reviewed jointly until consensus was achieved.

Methodological quality was assessed for all included studies using the Newcastle–Ottawa Scale (NOS), which evaluates three domains: selection of participants, comparability of study groups, and ascertainment of outcomes. Both reviewers performed this assessment independently and were blinded to each other's ratings; disagreements were resolved by discussion. The same independent, blinded, and consensus-based approach was used for both study selection and quality appraisal to minimize reviewer bias.

The certainty of evidence for each pooled outcome was assessed in accordance with the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework. This evaluation considered the risk of bias, inconsistency, indirectness, imprecision, and potential publication bias across the included studies. Evidence certainty was subsequently categorized as high, moderate, low, or very low, reflecting the overall confidence in the pooled estimates.

Statistical analyses were conducted using Review Manager (RevMan) version 5.4. A random-effects model was applied using the Restricted Maximum Likelihood (REML) estimation method, with Wald-type confidence intervals to account for inter-study variability. Pooled HR with corresponding 95% confidence intervals (CIs) were calculated, and statistical significance was set at $p < 0.05$. The random-effects model was applied regardless of the level of heterogeneity to ensure conservative and generalizable pooled estimates. Statistical heterogeneity was quantified using the I^2 statistic and assessed through Cochran's Q test. Forest plots were generated to visualize pooled effect estimates, and funnel plots, together with Egger's and Begg's tests, were used to explore potential publication bias.

Result

Work should be reported in SI units. Undue repetition in text and tables should be avoided. Comment on validity and significance of results is appropriate but broader discussion of their implication is

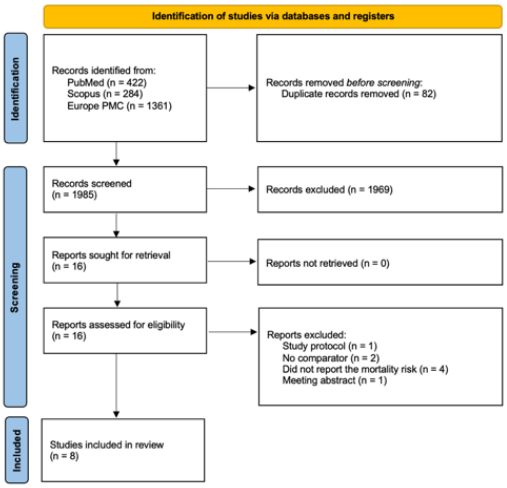

Figure 1. PRISMA flow diagram

A total of 1,985 records were identified through database searches, including PubMed (n = 422), Scopus (n =

284), and Europe PMC (n = 1,361). After removing 82 duplicate records prior to screening, 1,985 unique studies were screened for eligibility. Of these, 1,969 were excluded based on title and abstract review, leaving 16 reports sought for full-text retrieval, all of which were successfully obtained. Upon full-text assessment, six studies were excluded for reasons including being a study protocol (n = 1), lacking a comparator (n = 2), not reporting mortality risk (n = 4), or being a meeting abstract (n = 1). Ultimately, eight studies met all inclusion criteria and were included in the final systematic review (Figure 1).[3,4,11–16]

Across the eight included studies summarized in Table 2, sample sizes ranged widely from small single-center cohorts (Cooper et al., 2003; n = 109) to large national registries (Chertow et al., 2005; n = 40,538). Male representation was generally higher across studies, varying from approximately 52 % to 63 %. Mean or median patient ages spanned from the early 50s to the mid-60s, reflecting predominantly older adult and elderly dialysis populations. Study populations included diverse geographic and clinical settings: end-stage renal disease (ESRD) or chronic hemodialysis patients in Pakistan, Japan, China, Australia, and Brazil, as well as critically ill or acute kidney injury (AKI) cohorts on continuous renal replacement therapy (CRRT) in South Korea and the United States. Study periods ranged from the early 1990s to 2016, with most being retrospective cohort designs or follow-up observational analyses. The definitions of hypoalbuminemia varied slightly across studies, most often using thresholds between ≤ 3.5 g/dL and < 4.0 g/dL, though some studies stratified by albumin tertiles or broader categories.

Frequent comorbidities typical of dialysis populations, including diabetes (ranging from 17 % to 68 %), anemia (Hb < 11 g/dL), and chronic inflammation. Hemodialysis vintage and modality were noted in several studies, with median dialysis durations between 2 and 7 years in chronic HD populations and ≤ 3 months in incident ESRD cases. Average body mass indices were mostly in the normal-to-overweight range, while serum albumin levels averaged ~3.5 to 4.0 g/dL. Many cohorts were predominantly of one ethnicity (e.g., 86 % Caucasian in Thongprayoon et al., 2021), while others reflected local regional populations.

Table 2. Demographic characteristics of included studies

Study (Author, Year)	Sample Size (n)	Sex Distribution	Mean/Range of Age	Population / Setting	Albumin Cutoff for Hypoalbuminemia	Study Duration / Data Collection Period	Key Clinical Characteristics
Anees & Ibrahim (2006)	185	52.8% male, 47.2% female	Not reported	ESRD patients at Shalamar Hospital, Lahore, Pakistan	< 4.0 g/dL	June 2003 – October 2006	67.6% diabetes, 16.8% glomerulonephritis, 9.7% hypertension; 91.1% anemic (Hb <11 g/dL); 67% hypoalbuminemic
Moon et al. (2019)	1,581	60.5% male	63.2 ± 15.2 years	AKI patients on CRRT (South Korea)	Tertiles: ≤ 2.4 g/dL / 2.5–2.9 g/dL / ≥ 3.0 g/dL (lowest tertile ≤ 2.4 g/dL = hypoalbuminemic)	2010 – 2016	Differences across tertiles in AKI cause, dialysis dose, malignancy, hemoglobin, potassium, and APACHE II score; overall mortality 65.8%
Thongprayoon et al. (2021)	911	57 % male (520/911)	59.2 ± 14.9	Critically ill CRRT patients (USA)	≤ 2.4 / 2.5–2.9 / 3.0–3.4 / ≥ 3.5 g/dL	Dec 2006 – Nov 2015	86 % Caucasian; BMI 32.0 ± 15.8; no age or sex difference across albumin groups ($p > 0.05$); Caucasian proportion rose with higher albumin ($p = 0.002$). Severe hypoalbuminemia (≤ 2.4 g/dL) linked to highest mortality.
Tang et al. (2021)	447 total (Low ABL n = 151, Moderate n = 147, High n = 149)	62.3 % M (low), 61.2 % M (moderate), 62.4 % M (high)	63.9 ± 14.6 (low), 58.2 ± 15.3 (moderate), 52.0 ± 14.6 (high)	Chronic hemodialysis patients, China	Low ≤ 35.7 g/L (3.57 g/dL); Moderate 35.7 < ALB ≤ 38.9 g/L; High > 38.9 g/L	Retrospective; period not stated	Hemoglobin: 90 (73–106) g/L (low), 104 (90–116) g/L (moderate), 107 (95–119) g/L (high); RBC ($\times 10^{12}$/L): 3.33 (low), 3.6 (moderate), 3.68 (high); significant differences in age, Hb, and RBC ($p < 0.001$).
Iseki et al. (1997)	1,186 total (Died n = 342; Survived n = 844)	58.1 % male (55.3 % died; 59.2 % survived)	52.4 ± 0.4 (overall); 62.9 ± 0.7 (died); 48.8 ± 0.5 (survived)	Chronic HD patients, Okinawa, Japan	< 3.9 g/dL (mean albumin: 3.7 ± 0.03 died vs 4.0 ± 0.02 survived)	Baseline: January 1991; Follow-up through 1995	Mean serum albumin 3.9 ± 0.01 g/dL; diastolic BP 80.8 ± 0.4 mmHg (77.1 died vs 82.3 survived); diabetes 17.6 % overall (35.4 % died); BMI 21.6 ± 0.1 kg/m²; total protein 6.5 ± 0.02 g/dL; study linked low albumin and low DBP with increased mortality ($p < 0.0001$).

Study (Author, Year)	Sample Size (n)	Sex Distribution	Mean/Range of Age	Population / Setting	Albumin Cutoff for Hypoalbuminemia	Study Duration / Data Collection Period	Key Clinical Characteristics
Cooper et al. (2003)	109 total (PD = 52; HD = 57)	PD: 25F / 27M; HD: 22F / 35M	PD: 63.9 ± 1.8; HD: 57.7 ± 2.1	ESRD patients initiating dialysis (Australia)	Hypoalbuminemia defined as < 3.6 g/dL for HD and < 2.0 g/dL for PD	Not specified	Time on dialysis: PD 1.6 ± 0.2 months; HD 2.9 ± 0.3 months (p = 0.0003); no sex difference (p = 0.3); PD group older (p = 0.03). Study concluded hypoalbuminemia and protein malnutrition at dialysis initiation predicted increased morbidity and mortality.
Chertow et al. (2005)	40,538 total; Prealbumin group: 7,815 (19.3%)	51.0 % female (with prealbumin); 51.3 % (without)	61.5 ± 15.1 (with prealbumin); 60.3 ± 15.1 (without)	Chronic hemodialysis patients on thrice-weekly HD, USA	Prealbumin categorized a priori into 7 groups: <15, 15–20, 20–25, 25–30, 30–35, 35–40, ≥40 mg/dL	Labs averaged from final 3 months of 1997; cohort as of Jan 1, 1998	46.3 % Caucasian in prealbumin group vs 35.2 % in non-prealbumin; mean difference in age significant (p < 0.0001); used averaged lab values for exposure; lower prealbumin strongly associated with increased mortality and hospitalization risk.
Antunes et al. (2016)	221 (from 275 invited)	59 % male (130/221)	Median 50 (IQR 38–63)	Adult HD patients, two dialysis centers in Maceió, Brazil (INRV-SCMM & CDR-Sanatorium)	< 3.8 g/dL (hypoalbuminemia)	13-month prospective follow-up	Median HD vintage 7 years (IQR 4–9); diabetes 29 %; mean Hb 10.6 ± 1.9 g/dL; CRP 1.0 (0.19–1.29) mg/dL; ferritin 424.8 ng/mL; transferrin saturation 29.8 ± 10.6 %; hypoalbuminemia and high CRP predicted hospitalization; 4.9 % had temporary catheter at baseline.

The pooled overall effect estimate demonstrated no significant association between hypoalbuminemia and mortality among patients undergoing hemodialysis, with a combined hazard ratio (HR) of 1.08 (95% CI: 0.94–1.25, p = 0.28). Considerable heterogeneity was observed across studies (I^2 = 79%), indicating substantial variability in study outcomes (Figure 2).

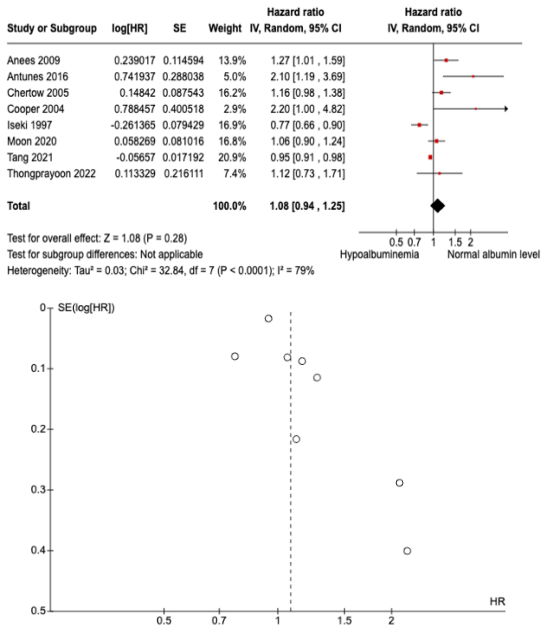

Figure 2. Meta-analysis showing an insignificant results of hypoalbuminemia to predict mortality in patients undergoing hemodialysis.

The methodological quality of the included studies was evaluated using the NOS, as summarized in Table 3. Most studies demonstrated moderate to high quality, with total scores ranging from 6 to 9 out of 9 possible points. Overall, five studies were rated as low risk of bias, while three showed moderate risk, indicating generally reliable study designs across the included literature. GRADE analysis for certainty assessment was also to appear moderate – low risk of bias.

Table 3. Newcastle–Ottawa Scale (NOS) assessment for risk of bias

Study (Author, Year)	Selection	Comparability	Outcome / Exposure	Total Score	Risk of Bias
Anees & Ibrahim (2006)	★★★	★	★★	**6 / 9**	Moderate
Moon et al. (2019)	★★★★	★★	★★★	**9 / 9**	Low
Thongprayoon et al. (2021)	★★★★	★★	★★	**8 / 9**	Low
Tang et al. (2021)	★★★	★★	★★	**7 / 9**	Moderate
Iseki et al. (1997)	★★★★	★★	★★★	**9 / 9**	Low
Cooper et al. (2003)	★★★	★	★★	**6 / 9**	Moderate
Chertow et al. (2005)	★★★★	★★	★★★	**9 / 9**	Low
Antunes et al. (2016)	★★★	★★	★★	**7 / 9**	Moderate

Table 4. GRADE Summary of Findings Framework

Outcome	No. of Studies	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Certainty of Evidence	Summary of Findings
Demographic characteristics of dialysis patients	8	⊕⊕○○	⊕⊕⊕○	⊕⊕⊕⊕	⊕⊕⊕⊕	⊕⊕⊕⊕	Moderate (⊕⊕⊕○)	Populations were predominantly male, middle to older age, with high prevalence of diabetes and hypertension.
Prevalence of hypoalbuminemia	8	⊕⊕○○	⊕⊕○○	⊕⊕⊕○	⊕⊕⊕○	⊕⊕○○	Moderate (⊕⊕⊕○)	Hypoalbuminemia prevalence ranged from 60–75%, depending on albumin cutoff (≤2.4–4.0 g/dL).
Association between hypoalbuminemia and mortality	8	⊕⊕○○	⊕○○○	⊕⊕⊕○	⊕⊕○○	⊕⊕○○	Low (⊕⊕○○)	Pooled analysis showed no significant association (HR 1.08, 95% CI: 0.94–1.25, p = 0.28).
Overall quality of evidence	—	—	—	—	—	—	Moderate to Low (⊕⊕–⊕⊕⊕○)	Evidence limited by observational design and heterogeneity; demographic and prevalence data consistent, but mortality findings uncertain.

Discussion

The demographic characteristics summarized in this review reflect considerable variability across populations, geographic regions, and dialysis modalities. Participants' ages ranged from middle-aged to elderly, with male predominance observed in most cohorts, consistent with the known higher prevalence of CKD and ESRD in men. Studies conducted across diverse regions, including South Asia, East Asia, Australia, North America, and South America, highlighted differences in comorbidities, such as diabetes, hypertension, and cardiovascular disease, which are known contributors to both CKD progression and adverse outcomes. These findings align with previous epidemiological data indicating that CKD prevalence increases with age and comorbidity burden, and that metabolic and vascular alterations contribute to disease progression.[17–19] CKD and dialysis profoundly affect homeostatic regulation, particularly in cardiovascular and metabolic systems, which may explain demographic patterns of risk and survival observed among the included cohorts.[20]

Regarding hypoalbuminemia, the present systematic review and meta-analysis found wide variation in the definitions and thresholds used across studies, ranging from ≤2.4 g/dL in critically ill patients to <4.0 g/dL in stable hemodialysis cohorts. The prevalence of hypoalbuminemia was consistently high, reinforcing its role as a marker of poor nutritional and inflammatory status. Supporting evidence from prior studies indicates that serum albumin reflects not only protein-energy malnutrition but also systemic inflammation and capillary leak, both of which are prevalent in dialysis patients.[21–23] However, some conflicting data exist, particularly in acute kidney injury populations where transient hypoalbuminemia may not carry the same prognostic weight as in chronic dialysis patients.[24,25] Albumin serves multiple physiological functions, it maintains oncotic pressure, binds endogenous and exogenous molecules, and possesses antioxidant properties.[24] Thus, explaining why reduced levels reflect both disease severity and impaired homeostasis.

The pooled results of this meta-analysis revealed that hypoalbuminemia was not significantly associated with increased mortality among dialysis patients, with a combined HR of 1.08 (95% CI 0.94–1.25, p = 0.28). This finding contrasts with earlier literature where low albumin was a strong independent predictor of mortality, possibly reflecting variations in patient selection, dialysis adequacy, and advances in supportive care over time.[26,27] Some supporting studies, such as those by Iseki et al. (1997) and Tang et al. (2021), did demonstrate associations between lower albumin and adverse outcomes, while others, including

Moon et al. (2019) and Thongprayoon et al. (2021), reported no significant relationship after adjustment for confounders.[4,12,14,14] From a physiological and pathophysiological perspective, mortality in dialysis patients is multifactorial, where albumin may act more as a surrogate marker than a direct cause. Hence, while hypoalbuminemia remains an important indicator of clinical frailty and systemic illness, its predictive value for mortality may be attenuated in contemporary dialysis populations.[28]

Study Limitations

This review has several limitations that should be considered when interpreting the findings. First, there was significant heterogeneity among the included studies in terms of population characteristics, albumin cutoff definitions, dialysis modalities, and study designs, which may have influenced the pooled estimates. Second, most included studies were observational and retrospective, making them subject to selection bias, confounding, and incomplete data reporting. Additionally, several studies lacked standardized methods for assessing nutritional or inflammatory status, limiting comparability across cohorts. Publication bias cannot be excluded, as studies reporting null associations between albumin and mortality may have been underrepresented.[29,30] Finally, the meta-analysis included studies spanning multiple decades, during which dialysis techniques and patient management strategies have evolved, potentially affecting mortality outcomes and albumin levels.

Conclusion

This systematic review and meta-analysis demonstrated that while hypoalbuminemia remains a frequent finding among patients undergoing hemodialysis, its association with mortality was not statistically significant when data were pooled across studies. Despite this, albumin continues to serve as a critical marker of nutritional and inflammatory status in dialysis populations and should be interpreted within the broader context of patient comorbidities and treatment adequacy. These findings underscore the multifactorial nature of mortality in renal replacement therapy, suggesting that albumin alone may not be a sufficient predictor of survival. Future prospective studies with standardized definitions, adjustment for confounders, and longitudinal assessment of nutritional and inflammatory parameters are warranted to clarify the prognostic value of serum albumin in contemporary dialysis care.

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