Review Article
Incidence and influencing factors for hypoglycemia in maintenance hemodialysis patients with diabetic kidney disease: a meta-analysis

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Abstract: The objective of this study was to evaluate the incidence of hypoglycemia in patients with diabetic kidney disease (DKD) undergoing maintenance hemodialysis (MHD) and to identify key factors influencing its occurrence. A comprehensive literature search was conducted across databases including CNKI, Wanfang data, VIP, SinoMed, PubMed, Cochrane Library, Web of Science and Embase from their inception to March 31, 2023. The search focused on studies addressing the incidence and influencing factors for hypoglycemia in DKD patients receiving hemodialysis. Eligible studies were selected based on predefined inclusion and exclusion criteria, and data were analyzed using Stata 15.0 software. A total of 24 studies involving 2388 patients were included in this meta-analysis, with 22 studies from China and 2 studies from English-speaking countries. The findings indicated that the incidence of hypoglycemia among hemodialysis patients with DKD was 41.7% (95% confidence interval (*CI*): 32.6% to 50.9%). Influencing factors associated with hypoglycemia in hemodialysis patients with DKD included age (odds ratio (OR) = 4.507, 95% *CI*: 3.272 to 6.209), course of DKD (*OR* = 3.547, 95% *CI*: 2.523 to 4.988), use of oral hypoglycemic drugs (*OR* = 4.643, 95% *CI*: 2.566 to 8.402), fasting plasma glucose (FPG) levels (risk ratio (RR) = 4.033, 95% *CI*: 2.594 to 6.269), insulin use (*OR* = 8.242, 95% *CI*: 4.517 to 15.042), application of glucose-free dialysate (*RR* = 7.987, 95% *CI*: 4.605 to 13.855), coefficient of variation in blood glucose (CVBG) (*OR* = 3.241, 95% *CI*: 2.071 to 5.071), mean blood glucose (MBG) (*OR* = 2.930, 95% *CI*: 1.635 to 5.248), medication compliance (*OR* = 4.300, 95% *CI*: 2.047 to 9.031) and self-care ability (*OR* = 3.543, 95% *CI*: 1.766 to 7.108). Specifically, risk factors identified were age > 60 years, DKD course > 1 year, use of oral hypoglycemic drugs, FPG < 6.1 mmol/L, insulin administration before dialysis, application of glucose-free dialysate, CVBG ≥ 0.26, MBG < 8.92 mmol/L, poor medication compliance, and poor self-care ability.

Keywords: DKD, hypoglycemic, hypoglycemia, influencing factors, meta-analysis

Introduction

Maintenance hemodialysis (MHD) is the primary modality of renal replacement therapy for patients with diabetic kidney disease (DKD) who progress to chronic renal failure in the uremic stage [1]. Patients with DKD undergoing MHD are at a higher risk of hypoglycemia compared to non-DKD patients due to several factors, including changes in hemodynamics, metabolic disorders, decreased renal clearance of insulin, glucose loss, malnutrition, and impaired gluconeogenesis [2, 3]. Hypoglycemia during hemodialysis is associated with various complications, such as inadequate dialysis, irreversible damage to heart and brain cells, and increased incidence and mortality of cardiovascular diseases. Recurrent hypoglycemic episodes can also lower the threshold for the sympathetic adrenal response, thereby increasing the risk of progressive cognitive impairment in elderly patients [4, 5]. Current studies on the

Table 1. PubMed retrieval strategy

Step	Strategy
#1	(Diabetic Nephropathies[MeSH Terms]) OR (Diabetic Nephropathy[Title/Abstract] OR Diabetic Kidney Disease*[Title/Abstract] OR Diabetic[Title/Abstract])
#2	(Renal Dialysis[MeSH Terms]) OR (Renal Dialyses[Title/Abstract] OR Hemodialysis[Title/Abstract] OR Hemodialyses[Title/Abstract] OR Dialysis[Title/Abstract])
#3	(Hypoglycemia[MeSH Terms]) OR (Glycopenia[Title/Abstract] OR Glucopenia[Title/Abstract] OR Low Blood Sugar[Title/Abstract] OR Low Blood Glucose[Title/Abstract])
#4	#1 AND #2 AND #3

incidence of hypoglycemia in DKD patients are mostly single-center with small sample sizes, leading to significant differences in incidence rates, ranging from 2.9% to 50.2% [6, 7]. Furthermore, there remains a lack of consensus on the factors that influence the development of hypoglycemia in this patient population. Given the clinical importance of managing hypoglycemia in DKD patients on MHD, a comprehensive understanding of its incidence, mechanisms, and influencing factors is crucial. Therefore, we systematically evaluated the incidence and main influencing factors for hypoglycemia in DKD patients undergoing MHD, thereby providing robust evidence to inform effective hypoglycemia management strategies. This study was conducted following the PRISMA statement, and the research protocol was registered on the PROSPERO database (registration number: CRD42023429239).

Materials and methods

Literature retrieval strategy

A comprehensive literature search was performed using the following databases: CNKI, Wanfang Data, VIP, SinoMed, PubMed, the Cochrane Library, Web of Science, and Embase. The search encompassed both subject headings and free-text terms, aiming to identify relevant studies and to trace references for additional pertinent literature. The timeframe for the literature search extended from the establishment of each database to March 31, 2023. Keywords used in the search included "Diabetic Nephropathies", "Diabetic Nephropathy", "Diabetic Kidney Disease", "Diabetic", "Renal Dialysis", "Renal Dialyses", "Hemodialysis", "Hemodialyses", "Dialysis", "Hypoglycemia", "Glycopenia", "Glucopenia", "Low Blood Sugar", and "Low Blood Glucose". The detailed retrieval strategy is shown in **Table 1**.

*Inclusion and exclusion criteria of literature*

(1) Studies were included if they met the following criteria: ① studies involving DKD patients; ② research focused on the incidence and influencing factors of hypoglycemia during hemodialysis; ③ study designs including randomized controlled trials (RCTs), cohort studies, and case-control studies; ④ literature reporting the occurrence of hypoglycemia (defined as blood glucose ≤ 3.9 mmol/L measured by a blood glucose meter) and its influencing factors, allowing direct extraction or calculation of odds ratios (OR), risk ratios (RRs), and 95% confidence intervals (CI); ⑤ publications in Chinese or English.

(2) The following articles were excluded: ① studies calculating the incidence of hypoglycemia by example; ② studies with insufficient or erroneous data that preclude extraction; ③ duplicate publications; in such cases, only studies with large sample sizes and detailed data were retained; ④ studies for which the full text could not be obtained; ⑤ studies deemed to be of low quality after evaluation; ⑥ review, conference papers, expert comments, and case reports.

Literature screening, data extraction, and quality evaluation

The screening, data extraction, and quality evaluation were independently completed by two researchers (Feifei Jiang and Hang Xu). Discrepancies were resolved through discussion or by consulting a third researcher. Literature management was performed using NoteExpress software. Preliminary literature screening involved a review of titles and abstracts, followed by full-text reading to determine final inclusion. Data extraction included details such as the first author, publication
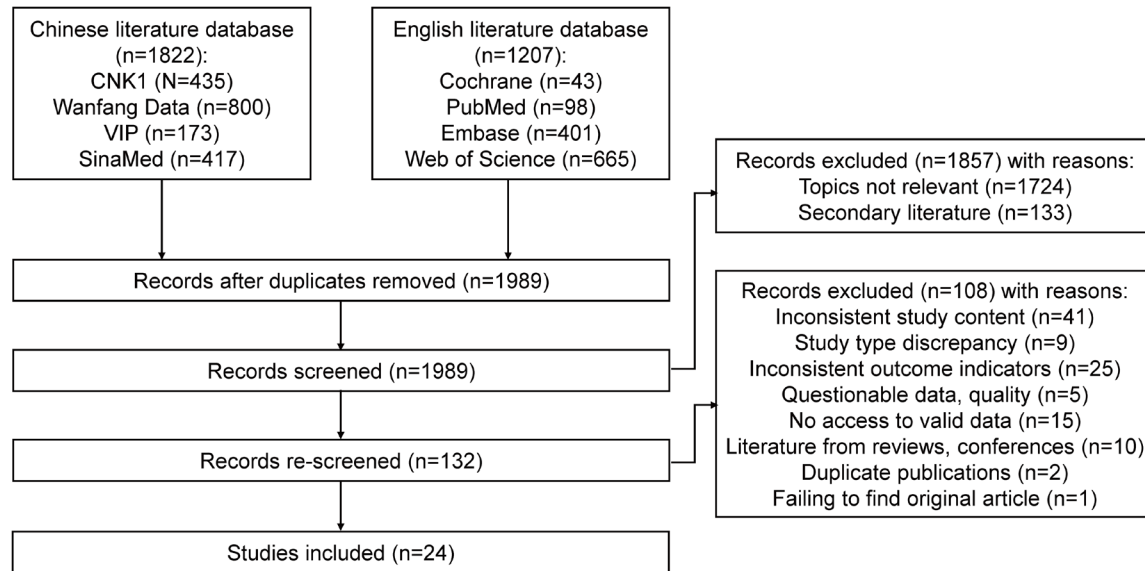
Figure 1. Literature selection process.

year, country/region, research type, sample size, incidence of hypoglycemia, and influencing factor OR/RR values with corresponding 95% CIs. Another analyst subsequently verified the extracted data independently. The quality of RCTs was assessed using the Jadad evaluation scale [8], which evaluates the generation of random sequences, allocation concealment, blinding, and withdrawals/dropouts, with a score of less than 4 indicating low quality and a score of 4 or higher indicating high quality. For cohort and case-control studies, the Newcastle Ottawa Scale (NOS) [9] was employed, which assesses aspects such as population selection, inter-group comparability, and exposure or outcome measures. A score of ≤ 4 indicates low quality, 5-6 indicates moderate quality, and ≥ 7 indicates high quality.

Statistical analysis

The incidence of hypoglycemia in hemodialysis patients with DKD and the corresponding OR/RR values and 95% CI for influencing factors were analyzed using Stata15.0 software. Effect sizes were pooled using either a fixed-effects or random-effects model based on heterogeneity assessment. Heterogeneity among studies was evaluated using the chi-square (χ^2) test (significance level $\alpha = 0.10$) and the I^2 statistic. An I^2 value of < 50% and a P value of > 0.10 were considered indicative of moderate homogeneity, in which a fixed-effects model was used for

the meta-analysis. Conversely, an I^2 value of ≥ 50% or a P value of ≤ 0.10 indicated significant heterogeneity, prompting the use of a random-effects model. In the case of heterogeneity, subgroup analyses and sensitivity analyses were conducted to explore potential sources and assess the stability of the pooled incidence rates and influencing factors. Publication bias was evaluated using funnel plots, Egger's tests, and Begg's tests, with a significance level of $\alpha = 0.05$.

Results

Literature search results

A total of 3029 articles were retrieved from 8 databases following the initial search. After removing duplicates using NoteExpress software, a re-screening was carried out according to the inclusion and exclusion criteria. After excluding ineligible studies, 24 articles were ultimately included (**Figure 1**).

Basic characteristics and quality evaluation

The characteristics and quality evaluation of the included studies are summarized in **Table 2**. Among the 24 studies, 22 were published in Chinese and 2 in English. The studies included 8 RCTs, 8 case-control trials, and 8 cohort trials, involving a total of 2388 patients. **Table 3** provides detailed information on the distribu-

Table 2. Basic information of included literature

| Author | Year of publication | Area | Study type | Sample capacity | | The incidence of hypoglyce-mia (%) | Influenc-ing factor | Literature quality rating |
				Case/Exposure/T	Comparison/C			
Chen Li [10]	2023	Hainan	Case control	58	62	48.33	①②③⑦	8[b]
Lei Jiandong [11]	2022	Leshan	Case control	112	130	53.71	⑦⑧⑨⑩	8[b]
Nian Sujuan [12]	2021	Hangzhou	Case control	46	40	53.49	⑦⑧⑨⑩	7[b]
Liu Zipu [13]	2021	Hebei	Case control	46	46	-	①②③	5[b]
Li Lishuang [14]	2019	Guangdong	Case control	40	40	-	①②③	6[b]
Yu Ge [15]	2018	Qinghai	Cohort study	50	62	44.64	①⑤	8[b]
Qian Feng [7]	2018	Jiangxi	Cohort study	32	64	62.50	-	6[b]
Gianchandani [16]	2018	America	Case control	76	74	50.67	-	7[b]
Cao Weibo [17]	2017	Shandong	RCT	22	24	-	⑥	5[a]
Aiyitan Ayithazi [18]	2017	Xinjiang	RCT	81	81	-	⑥	4[a]
Sun Yuanbo [19]	2016	Heilongjiang	Cohort study	18	48	27.27	④	8[b]
Wu Han [20]	2016	Anhui	RCT	35	35	-	⑤	4[a]
Chen Qingyun [21]	2015	Henan	RCT	20	22	-	⑥	4[a]
Li Yuxia [22]	2014	Guangdong	Case control	56	244	18.67	①②③	6[b]
Zhang Shouqing [23]	2014	Henan	Cohort study	59	58	-	⑥	7[b]
Zhang Yanli [24]	2013	Hebei	RCT	68	57	-	⑤	5[a]
Li Xiaoyan [25]	2013	Jiangxi	RCT	40	40	-	⑥	5[a]
He Xiaolan [26]	2011	Changsha	Cohort study	15	43	29.31	④	7[b]
Chen Li [27]	2010	Henan	Cohort study	9	16	44.00	⑤	6[b]
Liu Jiang [28]	2009	Ningbo	Case control	31	31	25.81	-	6[b]
Sun [29]	2009	Taiwan	Cohort study	54	48	52.94	-	8[b]
Zhang Li [30]	2008	Xi'an	RCT	48	46	-	⑥	4[a]
Huang Yuqing [31]	2008	Jiangxi	RCT	15	15	-	⑥	4[a]
Feng Xuefang [32]	2007	Shanghai	Cohort study	17	38	32.72	④	7[b]

Note: ① Age; ② DKD course; ③ Oral hypoglycemic drugs; ④ Fasting plasma glucose (FPG); ⑤ Insulin use; ⑥ Sugar free dialysate; ⑦ Coefficient of variation in blood glucose (CVBG = standard deviation of blood glucose/MBG); ⑧ Mean blood glucose (MBG); ⑨ Medication compliance; ⑩ Self-care ability; - indicates no relevant data or inability to perform quantitative synthesis; A is the Jadad score, and b is the NOS score.

tion of patient numbers, ages, and genders for each study.

Meta-analysis results

Meta-analysis of the incidence of hypoglyce-mia in DKD patients undergoing MHD: Of the 24 studies, 13 provided data suitable for meta-analysis of the hypoglycemia incidence in DKD patients undergoing MHD. Given the heterogeneity observed among the included studies (I^2 = 92%), a random-effects model was used. The results showed that the incidence of hypoglycemia in DKD patients undergoing MHD was 41.7% (95% CI: 32.6% to 50.9%), as shown in **Figure 2**.

Subgroup analysis of the incidence of hypoglycemia in DKD patients undergoing MHD: Subgroup analyses were conducted based on research type and publication year. For cohort studies (n = 7), the heterogeneity was high (I^2 = 75.6%, P < 0.001), with a calculated hypoglyce-

mia incidence of 41.3% (95% CI: 32.1-50.6). For case-control studies (n = 6), the heterogeneity was substantial (I^2 = 95.9%, P < 0.001), with a calculated hypoglycemia incidence of 41.9% (95% CI: 26.4-57.4). When stratified by publication year, 6 articles published within the last 5 years (I^2 = 0.0, P = 0.425) revealed a hypoglycemia incidence of 51.2% (95% CI: 47.6-54.8), whereas 7 articles published over five years ago showed significant heterogeneity (I^2 = 86.6, P < 0.001) and an incidence of 32.5% (95% CI: 21.7-43.2) (**Table 4**).

Meta-analysis of influencing factors: Among the 24 studies, 20 were eligible for quantitative analysis, identifying 10 extractable influencing factors. These factors were analyzed and their OR/RR values and 95% CI were pooled. The final meta-analysis identified the following risk factors for hypoglycemia in DKD patients undergoing MHD: age ≥ 60 years (I^2 = 48.5, *P* = 0.101; OR/RR: 4.20, 95% CI: 3.00-5.89, *Z* =

Table 3. Total number of patients included in the study, gender distribution, age

Author	Year of publication	Number of patient cases	Male	Female	Average age (years)
Chen Li [10]	2023	120	76	44	52.7±8.5
Lei Jiandong [11]	2022	242	135	107	NI
Nian Sujuan [12]	2021	86	55	31	65.1±11.3
Liu Zipu [13]	2021	46	NI	NI	NI
Li Lishuang [14]	2019	160	80	80	NI
Yu Ge [15]	2018	112	84	28	NI
Qian Feng [7]	2018	96	56	40	NI
Gianchandani [16]	2018	150	79	71	60.4±14.0
Cao Weibo [17]	2017	46	32	14	NI
Aiyitan Ayithazi [18]	2017	162	84	29	61.5±7.5
Sun Yuanbo [19]	2016	66	37	29	55.0±12.2
Wu Han [20]	2016	70	46	24	54.7±12.0
Chen Qingyun [21]	2015	42	27	15	56.8±6.0
Li Yuxia [22]	2014	300	169	131	NI
Zhang Shouqing [23]	2014	117	72	45	NI
Zhang Yanli [24]	2013	125	72	53	60.6±10.7
Li Xiaoyan [25]	2013	80	44	36	66.4±4.9
He Xiaolan [26]	2011	58	36	22	NI
Chen Li [27]	2010	25	13	12	62.2±12.9
Liu Jiang [28]	2009	31	18	13	61.3±9.5
Sun [29]	2009	102	60	42	64.1±10.9
Zhang Li [30]	2008	94	52	42	65.2±7.4
Huang Yuqing [31]	2008	30	15	15	NI
Feng Xuefang [32]	2007	55	26	29	NI

Note: NI, no information.

8.334, P < 0.001), DKD course > 1 year (I^2 = 0.0, P = 0.464; OR/RR: 3.55, 95% CI: 2.52-4.99, Z = 7.281, P < 0.001), use of oral hypoglycemic drugs (I^2 = 67.2, P = 0.028; OR/RR: 4.64, 95% CI: 2.57-8.40, Z = 5.073, P < 0.001), FPG < 6.1 mmol/L (I^2 = 0.0, P = 0.986; OR/RR: 4.03, 95% CI: 2.59-6.27, Z = 6.196, P < 0.001), pre-dialysis insulin use (I^2 = 0.0, P = 0.714; OR/RR: 8.24, 95% CI: 4.52-15.04), Z = 6.196, P < 0.001), use of glucose-free dialysate (I^2 = 18.5, P = 0.289; OR/RR: 7.99, 95% CI: 4.61-13.86, Z = 7.395, P < 0.001), CVBG ≥ 0.26 (I^2 = 0.0, P = 0.590; OR/RR: 3.24, 95% CI: 2.07-5.07, Z = 5.147, P < 0.001), MBG < 8.92 mmol/L, poor medication adherence (I^2 = 0.0, P = 0.545; OR/RR: 2.93, 95% CI: 1.64-5.25, Z = 5.147, P < 0.001), and poor caring ability (I^2 = 0.0, P = 0.810; OR/RR: 3.54, 95% CI: 1.77-7.11, Z = 3.561, P < 0.001) (**Table 5**).

Sensitivity analysis: Due to the significant heterogeneity observed in the incidence of hypoglycemia among DKD patients undergoing MHD, a sequential exclusion method was used for sensitivity analysis. Following the exclusion of certain studies, the results showed that the incidence of hypoglycemia was 40.2% to 42.9%, which was similar to the previously reported figure of 41.7%. This finding indicates that the meta-analysis results are relatively robust. In the analysis of influencing factors, the heterogeneity associated with oral hypoglycemic drugs was found to be 67.2%. A sensitivity analysis was conducted using the same method, and the combined effect values did not show substantial change, further supporting the stability of the meta-analysis results (**Figures 3** and **4**).

*Publication bias:* Assessment of publication bias using a funnel plot for the incidence of hypoglycemia showed asymmetry among the study points. However, Begg's test (Z = 1.04, P = 0.300) and Egger's test (t = 1.50, P = 0.161) did not suggest publication bias (**Figure 5**).

Discussion

Higher incidence of hypoglycemia in DKD patients undergoing MHD

DKD is a leading cause of end-stage kidney disease. Over the past two decades, data on dialysis in China show a rising proportion of DKD as the underlying cause of end-stage kidney disease [33]. Hypoglycemia is a prevalent acute complication in DKD patients undergoing hemodialysis. International studies have reported that the incidence of hypoglycemia during dialysis is 23.8% to 47.6% [6, 7], whereas studies from China have shown a significantly higher range of 34.4% to 62.5%, compared to 12.5%
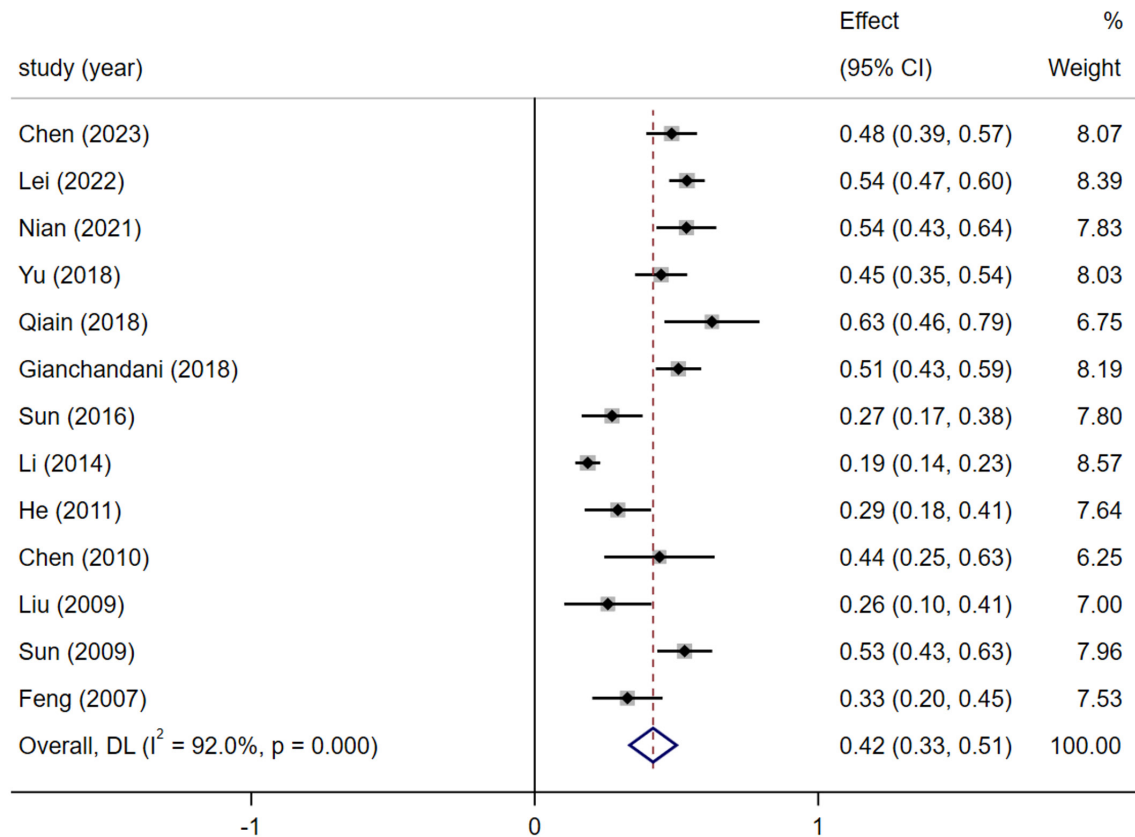
Figure 2. Forest plot of maintenance hemodialysis (MHD).

Table 4. Subgroup analysis of hypoglycemia incidence in DKD patients undergoing MHD

Different research types	Number of studies included	Heterogeneity test		Effect model	The incidence of hypoglycemia (%) (95% CI)
		I^2 (%)	P		
Study type					
Cohort study	7 [7, 15, 19, 26, 29, 31, 32]	75.6	< 0.001	Random	41.3 (32.1-50.6)
Case-control study	6 [10-12, 16, 22, 28]	95.9	< 0.001	Random	41.9 (26.4-57.4)
Publication year of the paper					
Over the past 5 years (2018 to present)	6 [7, 10-12, 15, 16]	0.0	0.425	Regular	51.2 (47.6-54.8)
5 years ago (before 2018)	7 [19, 22, 26-29, 32]	86.6	< 0.001	Random	32.5 (21.7-43.2)

Note: MHD, maintenance hemodialysis; DKD, diabetic kidney disease; OR, odds ratio; RR, risk ratio; CI, confidence interval.

to 18.7% in non-DKD hemodialysis patients [7]. Moreover, the incidence of severe hypoglycemia in elderly patients (≥ 60 years) is in one study was alarmingly high at 87.5% [34]. Our meta-analysis revealed that the incidence of hypoglycemia during hemodialysis in DKD patients was 41.7% (95% CI: 32.6-50.9%). Given the heterogeneity across studies, further subgroup analyses were conducted based on the study design. Results showed a combined hypoglycemia incidence of 41.3% (95% CI: 32.1% to 50.6%) for seven cohort studies,

with a decrease in heterogeneity (I^2 = 75.6%), accounting for some heterogeneity. Additionally, studies published more than five years ago reported a hypoglycemia incidence of 32.5% (95% CI: 21.7% to 43.2%) in DKD patients undergoing dialysis, while recent studies reported a higher incidence of 51.2% (95% CI: 47.6% to 54.8%), with homogeneity among the studies. These findings suggest that variability in reported hypoglycemia incidence could be influenced by factors such as differences in monitoring methods, reporting selections, and

Table 5. Meta-analysis of the influencing factors of hypoglycemia in DKD patients undergoing MHD

Influencing factor	Number of studies included	Heterogeneity test		Effect model	OR/RR (95% CI)	Z	P
		I^2 (%)	P				
Age	5 [10, 13-15, 22]	48.5	0.101	Regular	4.20 (3.00-5.89)	8.334	< 0.001
DKD course	4 [10, 13, 14, 22]	0.0	0.464	Regular	3.55 (2.52-4.99)	7.281	< 0.001
Oral hypoglycemic drugs	4 [10, 13, 14, 22]	67.2	0.028	Random	4.64 (2.57-8.40)	5.073	< 0.001
FPG	3 [19, 26, 32]	0.0	0.986	Regular	4.03* (2.59-6.27)	6.196	< 0.001
Insulin use	4 [15, 20, 24, 27]	0.0	0.714	Regular	8.24 (4.52-15.04)	6.872	< 0.001
Sugar free dialysate	7 [17, 18, 21, 23, 25, 30, 31]	18.5%	0.289	Regular	7.99* (4.61-13.86)	7.395	< 0.001
CVBG	3 [10-12]	0.0	0.590	Regular	3.24 (2.07-5.07)	5.147	< 0.001
MBG	2 [11, 12]	0.0	0.545	Regular	2.93 (1.64-5.25)	3.614	< 0.001
Medication compliance	2 [11, 12]	48.3	0.164	Regular	4.30 (2.05-9.03)	3.852	< 0.001
Self-care ability	2 [11, 12]	0.0	0.810	Regular	3.54 (1.77-7.11)	3.561	< 0.001

Note: MHD, maintenance hemodialysis; DKD, diabetic kidney disease; OR, odds ratio; RR, risk ratio; CI, confidence interval; FPG, fasting plasma glucose; CVBG, Coefficient of variation in blood glucose; MBG, mean blood glucose; * represents the RR value, while the rest represent the OR value.
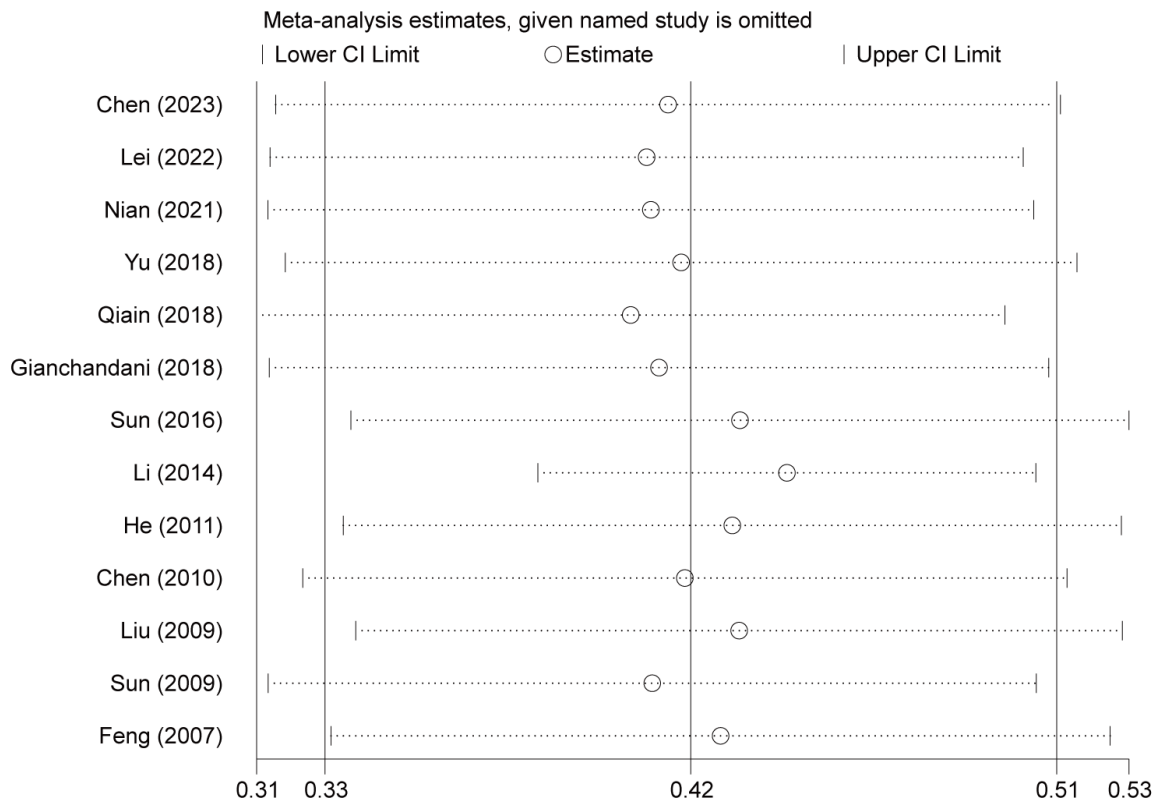

Figure 3. Sensitivity analysis of the incidence of maintenance hemodialysis (MHD)-associated hypoglycemia in patients with DKD.

the presence of asymptomatic hypoglycemia, which might lead to an underestimation of the true incidence and severity [35]. In addition, hypoglycemia, while often easier to correct than hyperglycemia, receives less preventive attention from patients. The International Hypoglycemia Study Group has pointed out that hypoglycemia is a risk factor for cardiovascular disease and death [36]. In recent years, medical practice has begun to emphasize the importance of hypoglycemia prevention, making it a key research focus.

Meta-analysis estimates, given named study is omitted
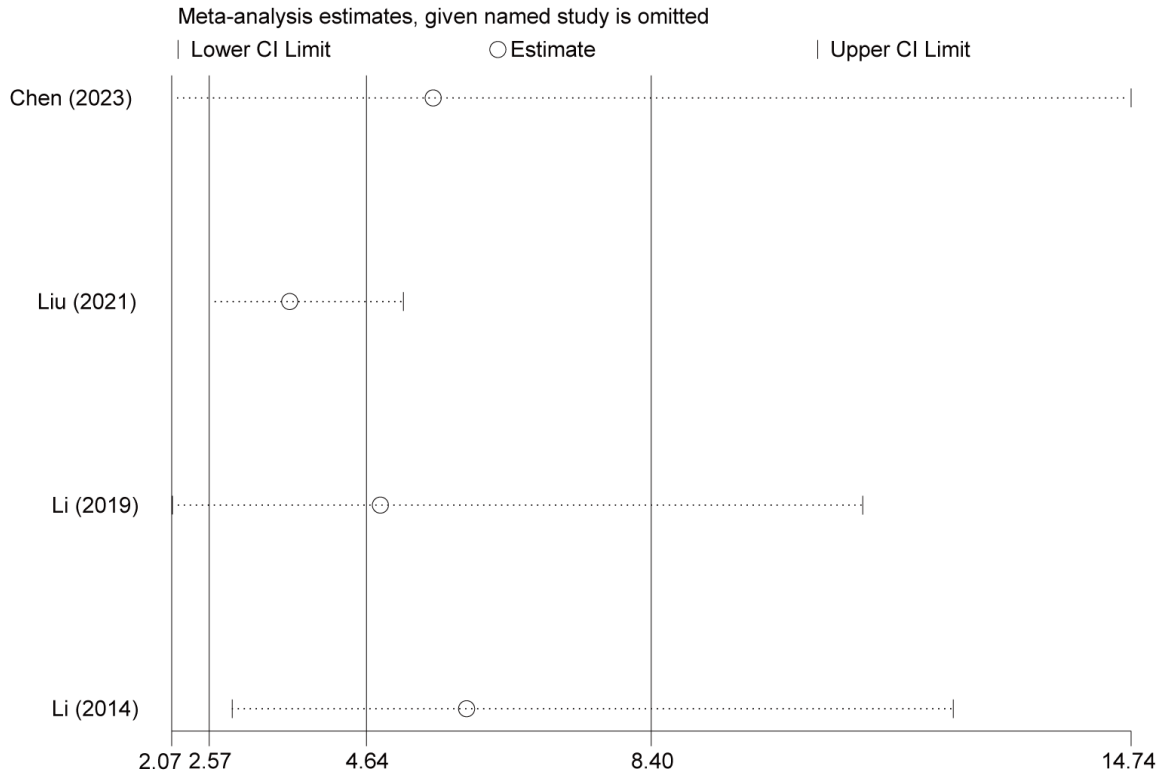
Figure 4. The susceptibility analysis of oral antidiabetic drugs.
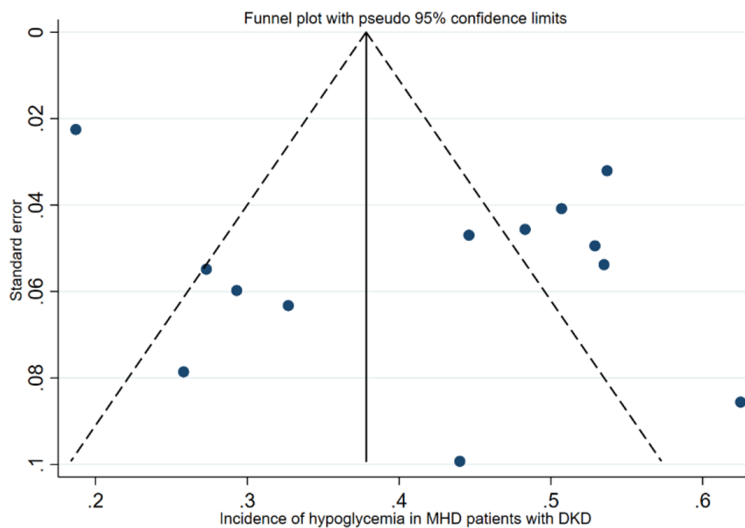
Figure 5. Funnel plot of maintenance hemodialysis (MHD)-associated hypoglycemia incidence rate in DKD patients.

Factors influencing hypoglycemia in DKD patients undergoing MHD

(1) Age and course of DKD: Epidemiological studies have shown that more than half of MHD patients are elderly. Elderly DKD patients often suffer from peripheral neuropathy, which impairs central nervous system response and reflex regulation to hypoglycemia, increasing the risk of asymptomatic hypoglycemia. This can lead to misdiagnoses such as cerebrovascular diseases, delaying appropriate treatment and resulting in more serious consequences [38, 39]. Moreover, a course of DKD exceeding one year can increase the risk of adrenal insufficiency, leading to reduced insulin degradation and glucocorticoid secretion, thereby contributing to lower blood glucose levels. Therefore, patients aged ≥ 60 years and with a DKD course > 1 year need more attention to prevent asymptomatic hypoglycemia.

(2) Oral hypoglycemic drugs: While previous meta-analyses indicated that hypoglycemic drugs have cardio-renal protection effects in

patients with type 2 diabetes [40, 41], their use may also lead to side effects of hypoglycemia, particularly in DKD patients with impaired renal drug metabolism. Hypoglycemic drugs are mainly metabolized by the kidneys, and this can easily lead to increased hypoglycemia risk during dialysis, especially in elderly patients with renal atrophy and reduced renal blood flow. This study included four original studies, and the results showed that patients who took oral hypoglycemic drugs on dialysis days had a 3.64-fold increased risk of hypoglycemia compared to those who did not. Caution is recommended in using these medications, particularly in light of guidelines [42] that contraindicate most oral hypoglycemic drugs, such as sulfonylureas and biguanides, in dialysis patients. Further research is necessary to explore the use of most traditional and novel oral hypoglycemic drugs in dialysis patients, as these medications often require dose adjustments or lack relevant evidence.

(3) Fasting plasma glucose (FPG): FPG levels are an important factor affecting blood glucose fluctuations. Hemodialysis induces U-shaped glucose fluctuations [43], similar to the FPG variation. Our findings showed that patients with an FPG level of < 6.1 mmol/L had a 4.03 times higher risk of hypoglycemia than those with an FPG of ≥ 6.1mmol/L. However, elevated PFG levels also increased the incidence of complications, such as infection. Thus, maintaining an FPG between 6.1 and 7 mmol/L appears optimal for minimizing the risks of hypoglycemia and other complications.

(4) Insulin use: Hypoglycemia during dialysis is closely related to insulin dosage and insulin resistance [44]. Although insulin resistance tends to improve in DKD patients, insulin's macromolecular nature makes it difficult to pass through dialysis membranes, extending the half-life of exogenous insulin. If the original insulin dose remain unchanged, there is an increased risk of hypoglycemia [45]. Therefore, insulin regimens for DKD patients on dialysis should be individualized and adjusted on dialysis days to prevent hypoglycemia.

(5) Glucose-free dialysate use: Our analysis revealed a 6.99-fold increased risk of hypoglycemia with the use of glucose-free dialysate. The gradient in glucose concentration between plasma and dialysate during dialysis promotes the diffusion of plasma glucose into the dialysate, leading to continuous glucose loss (15-30 g per session) [2]. With diminished renal gluconeogenesis, the risk of hypoglycemia is greatly increased [46]. Therefore, the use of glucose-free dialysate may cause hypoglycemia.

(6) Coefficient of variation in blood glucose (CVBG) and mean blood glucose (MBG): CVBG (standard deviation/MBG) and MBG can reflect the fluctuation of blood glucose [47]. Fluctuating blood glucose levels indicate poor glycemic control, which leads to poor prognosis. This study showed that patients with CVBG ≥ 0.26 and MBG < 8.92 mmol/L had a 2.24-fold and 1.93-fold increased risk of hypoglycemia, respectively. Elderly diabetic patients exhibited greater blood glucose variability and poorer hypoglycemia awareness [48], possibly leading to poor blood glucose management. Thus, careful monitoring of CVBG and MBG during patient treatment.

(7) Medication compliance and caring ability: Recent research has increasingly recognized the impact of psychosocial factors on hypoglycemia in dialysis patients with diabetes. As a chronic condition, kidney disease demands medication adherence and self-management, which are often intertwined with socio-economic status and self-care ability. DKD patients require adjustment to their hypoglycemic drugs or insulin dosages during hemodialysis. Individuals exhibiting poor medication adherence to prescribed hypoglycemic regimens are at an increased risk of hypoglycemia. Effective care involves both family support and self-management behaviors. A robust social support system is beneficial in fostering self-management behaviors among diabetic patients and enhancing their confidence in preventing hypoglycemia [49]. Conversely, patients with inadequate self-management levels tend to exhibit poor compliance. They struggle to effectively manage physical activity, monitor blood glucose, and adhere to medication and nutrition regimens, which increase their susceptibility to hypoglycemia [50]. Therefore, it is imperative to prioritize clinical evaluations in this context.

This study has several limitations: (1) Most of the studies included in this analysis are in Chinese, which may result in regional bias; (2) Research on the impact of CVBG, MBG, medi-

cation adherence, and self-care ability on hypoglycemia is relatively nascent, especially studies on medication adherence and care ability. In addition, the limited number of studies available may introduce bias, necessitating further high-quality investigations.

In summary, the incidence of hypoglycemia in DKD patients during hemodialysis is relatively high, with recent studies indicating an upward trend. Factors such as advanced age, a course of DKD exceeding 1 year, oral hypoglycemic drug use, an FPG level of less than 6.1 mmol/L, pre-dialysis insulin use, use of sugar-free dialysate, large blood glucose fluctuations, and poor medication compliance and caring ability are associated with increased risk of hypoglycemia. Strategies to mitigate these risks include adjusting hypoglycemic or insulin regimens on dialysis days, using sugar-containing dialysate, and implementing educational interventions and social support measures to improve patient compliance and self-care capabilities, ultimately improving patient outcomes.

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Disclosure of conflict of interest

None.

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