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Meta-analysis of Risk Factors for Pulmonary Infections in End-stage Maintenance Hemodialysis Patients

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Abstract: *The objective of this study was to conduct a systematic evaluation of the risk factors and causative flora associated with combined lung infections in maintenance hemodialysis patients with end-stage renal disease. A comprehensive search was conducted across multiple databases, including VIP, Wan Fang, CNKI, CBM, Embase, The Cochrane Library, Web of Science, and PubMed. The objective was to identify and collate information on the risk factors associated with combined lung infections in patients with chronic renal failure. Additionally, case-control and cohort studies on the risk factors of pulmonary infections in patients with chronic renal failure and the flora of infections were sought. Two independent evaluators conducted the literature screening, quality assessment, and data extraction. The meta-analysis was performed using Revman 5.4 and Stata 15.0 software. A total of 21 papers were included in the study, of which 17 were case-control studies, and four were cohort studies. The total number of patients included in the study was 3004, with 1018 of them having pulmonary infections, resulting in an infection rate of 33%. The proportion was 59%. A meta-analysis of 33 potential risk factors revealed that age, body mass index (BMI), history of diabetes mellitus, C-reactive protein (CRP), serum albumin (ALB), hemoglobin (HGB), urea reduction rate (URR), and urea clearance index (KT/V) were significantly associated with the development of pulmonary infections. Risk factors were identified as significant for developing combined lung infections in patients with end-stage renal disease (ESRD) undergoing maintenance hemodialysis (MHD): cardiothoracic ratio, disease duration, age at dialysis, average weekly dialysis time, and dialysis modality. The most prevalent bacteria associated with lung infections were gram-negative bacteria, with Klebsiella pneumoniae, Pseudomonas aeruginosa, and Hemophilus influenzae representing the top three in terms of prevalence. The most prevalent pathogens were Pseudomonas aeruginosa and Hemophilus influenzae. The incidence of pulmonary infections in maintenance hemodialysis patients with end-stage renal disease is high. Identifying risk factors for the development of lung infections in patients with this disease and the subsequent development of interventions can help reduce the prevalence of lung infections. Given the limitations of the quantity and quality of existing literature, further high-quality studies are needed to validate the above conclusions.*

Keywords: *Chronic renal failure, Maintenance hemodialysis, Pulmonary infection, Risk factors, Meta-analysis*

1. Introduction

End-stage renal disease (ESRD) is a severe condition that requires dialysis or kidney transplantation to sustain life. It is costly, disabling, and often shortens the patient's lifespan [1]. There has been an increase in the prevalence of treated ESRD worldwide, with studies suggesting that the number of patients with end-stage renal disease requiring renal replacement therapy is estimated to be between 4.902 million and 7.083 million [2], rapidly increasing the global burden of health and health care[3]. Maintenance hemodialysis (MHD) is defined as treatment for hemodialysis for at least 90 days. It has been documented that one in five patients is diagnosed with pneumonia within one year of starting hemodialysis treatment. The annual mortality rate of pulmonary infection in dialysis-treated patients with ESRD MHD is approximately 10 times higher than that of the general population [4-5], which is one of the severe pulmonary complications of ESRD MHD patients, significantly increasing the burden of medical costs and prolonging hospital stays. Therefore, it is essential to identify the risk factors of

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pulmonary infection in patients with ESRD and MHD as soon as possible and give corresponding medical measures. In recent years, literature searches at home and abroad have found that many researchers have paid extensive attention to and conducted clinical studies on the risk factors of pulmonary infection in patients with ESRD MHD. However, each study's risk factors and research results are different. There is a lack of scientific and reliable evidence-based evidence. Therefore, this article uses meta-analysis to integrate the risk factors of pulmonary infection in patients with ESRD MHD to provide a reference for effective prevention of pulmonary infection and clinical treatment of patients with ESRD MHD in the early stage of hospitals.

2. Materials and Methods

2.1. Literature Search Strategy

The databases of VIP, Wan Fang, CNKI, CBM, Embase, The Cochrane Library, Web of Science, and PubMed were searched to collect clinical studies on risk factors for pulmonary infection in patients with regular hemodialysis for chronic renal failure in China, and the search time limit was from the establishment of the database to January 19, 2024. Chinese search terms: chronic renal failure, uremia, azotemia, hemodialysis, renal dialysis, continuous renal replacement therapy, pulmonary infection, pneumonia, community-acquired pneumonia, community-acquired pneumonia, fungal pneumonia, bacterial pneumonia, influencing factors, risk factors, high-risk factors, correlations, predictors, etc. English search terms: Uremia, Chronic Kidney Failure, Renal Dialysis, Continuous Renal Replacement Therapy, Lung Infection, Pulmonary Infection, Pneumonia, Risk Factors, Root Cause Analysis, Correlation, etc. In addition, a snowball search and review of significant research literature were conducted to ensure that relevant literature was noticed.

2.2. Inclusion and exclusion criteria

(1) Inclusion criteria: ① patients diagnosed with end-stage renal disease; ② regular hemodialysis for at least 3 months; ③ pulmonary infection, and there is a clear diagnostic criteria for pulmonary infection; ④ Case-control study or cohort study. (2) Exclusion criteria: ① data extraction difficulties or data errors in the literature. ② Primary pulmonary diseases, such as pulmonary tuberculosis, chronic obstructive pulmonary disease, or combined with other infections, such as catheter-related infections, urinary tract infections, etc. ③ Literatures with Newcastle-Ottawa Scale (NOS) score < 5; ④ Non-Chinese or English literature.

2.3. Literature screening and data extraction

Two evaluators used Endnote 20 to independently screen the literature, extract the data, and cross-check the extraction results. In disagreement, it is checked and corrected with the third evaluator. The extracted data include: (1) General information: first author, publication time, research type, research years, research area; (2) Basic statistical data: total sample size, incidence of pulmonary infection, number of cases in pulmonary infection group and non-pulmonary infection group, influencing factors, related data of infected flora, outcome index data; (3) The elements of literature quality evaluation.

2.4. Quality evaluation of included studies

The literature quality evaluation of case-control and cohort studies was independently evaluated and cross-checked by two evaluators based on the recommended NOS scale [6]. In case of disagreement, the third evaluator is consulted for judgment. The NOS scale consists of 8 items, with a total score of 9 points, and 5-9 points are regarded as medium and high quality. This Meta-analysis excludes studies with NOS scores < 5 points [7].

2.5. Statistical analysis

Rev Man 5.4 software and Stata15.0 software were used for Meta-analysis. In 21 articles, ≥ 2 articles involving the same factors were statistically analyzed. The odds ratio (OR) nod 95% confidence interval (CI) were used as the effect size. I^2 was used to test the heterogeneity between studies. If $I^2 \geq 50$ %, it indicated moderate to high heterogeneity between studies. A random effect model was used, and sensitivity analysis was performed. If $I^2 < 50\%$, the heterogeneity between the studies is small, and the

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fixed effect model is used [8]. Funnel plot and Begg test were used to judge the bias of published literature in the literature with research factors ≥ 10 [9]. The test level of this study was $\alpha = 0.05$, and $P < 0.05$ was considered statistically significant.

3. Results

3.1. Literature search results

A total of 1538 articles were retrieved, including 1205 Chinese and 333 English articles. Eight hundred eighty-seven articles were obtained by using Endnote 20 software to remove duplicates. According to the inclusion and exclusion criteria, 21 articles [10-30] were finally included for meta-analysis. The literature screening process is shown in Figure 1.

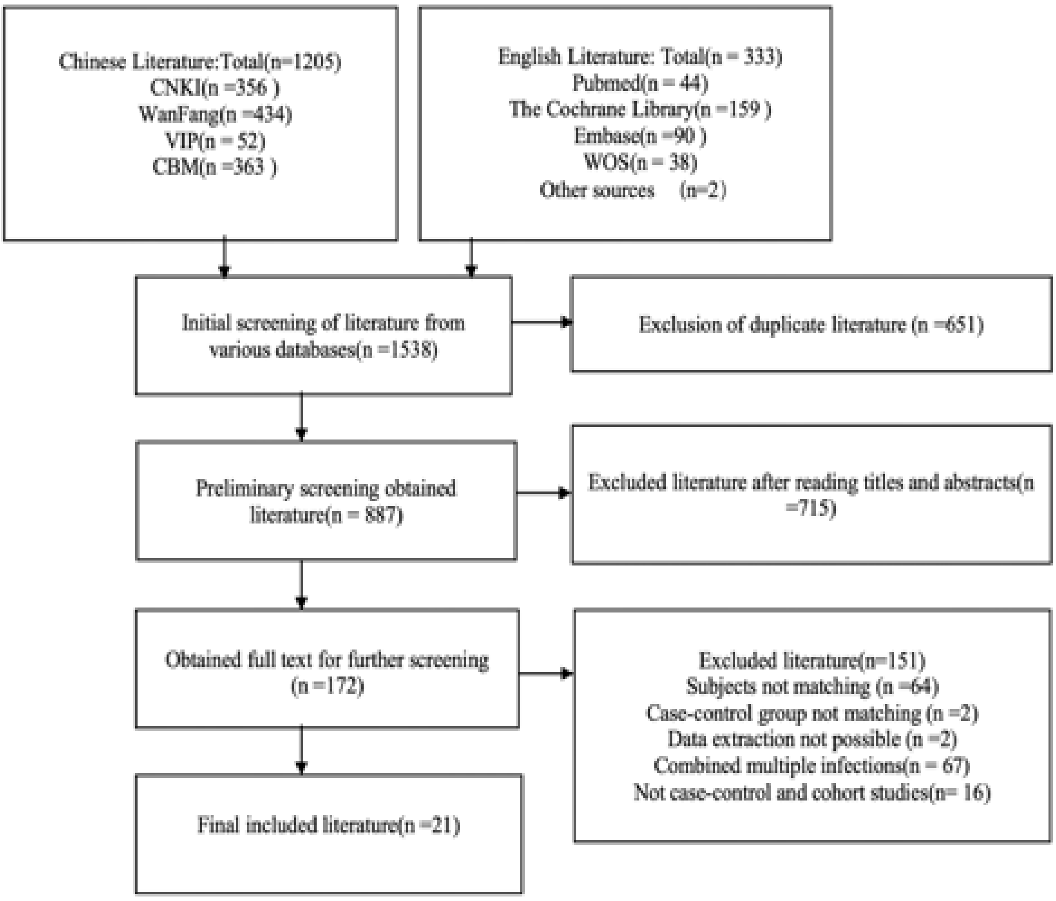

Figure 1: The flow chart of screening of literatures

3.2. Basic characteristics of the included literature

A total of 21 literatures [10-30] that met the inclusion and exclusion criteria were included in this study, including 17 case-control studies and 4 cohort studies, including 20 Chinese literature and 1 English literature. The NOS scale was used for scoring, and the quality scores of all literature were ≥ 5 points, as shown in Table 1. A total of 3004 ESRD MHD patients were included in this study. Among them, 1018 patients had a pulmonary infection, and 33 exposure factors were related, as shown in Table 1.

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Table 1: Basic information of included studies

Eligible Studies	Year	Research area	Research type	Pulmonary infection group (case)	Non-pulmonary infection group (case)	Pulmonary infection rate (%)	Exposure factors	NOS score (points)
Jie Ren et al. [10]	2023	Changzhou, Jiangsu	Case-control study	28	54	45.16	①⑤⑥⑦⑧⑨⑯㉑㉗㉚	7
Muzhou Qian et al. [11]	2017	Nantong, Jiangsu	Case-control study	40	40	50.0	①②⑤⑩⑪⑲	7
Pei Liu et al. [12]	2020	Xi'an, Shaanxi	Case-control study	42	92	31.34	①④⑤⑩⑪⑬⑭⑲㉖㉛	7
Hongying Ye et al. [13]	2018	Jinhua, Zhejiang	Case-control study	52	292	15.10	①②⑪⑫⑮㉗㉖㉜㉝	7

Continued from table 1: Basic information of included studies.

Eligible Studies	Year	Research area	Research type	Pulmonary infection group (case)	Non-pulmonary infection group (case)	Pulmonary infection rate (%)	Exposure factors	NOS score (points)
Yucai Zhai et al. [14]	2016	Beijing	Case-control study	52	119	41.94	①⑮⑯㉗	7
Ling Yuan et al. [15]	2022	Jingdezhen, Jiangxi	Case-control study	35	45	43.75	①⑤⑩⑪	7
Dongchi Zhou et al. [16]	2014	Pudong, Shanghai	Case-control study	46	91	33.58	①②⑤⑩⑪⑲	5
Bin Yan [17]	2014	Xichang, Sichuan	Case-control study	28	52	35.00	①④⑤⑪⑲	5
Jin Qiang Deng [18]	2018	Yunfu, Guangdong	Case-control study	58	67	46.40	①③⑪⑯⑱⑲㉗	6
Ningchuan Huang et al. [19]	2020	Guiyang, Guizhou	Case-control study	54	92	36.99	①③⑤⑬⑳㉗	6
Huanhao Liu et al. [20]	2007	Wuzhou, Guangxi	Case-control study	44	47	48.35	①④⑤⑪⑲	5
Xuebo Chen et al. [21]	2014	Zhoushan, Zhejiang	Case-control study	40	60	40.0	①③⑤⑪⑯⑱⑲	6
Dinghe Lei et al. [25]	2009	Guilin, Guangxi	Case-control study	46	40	48.0	①③④⑤⑪⑱⑲	7

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Ji Liang et al. [22]	2014	Haikou, Hainan	Case-control study	40	40	50.0	①②③⑤⑪⑯⑱⑲㉗	6
Yongjin Zhou et al. [23]	2021	Shangrao, Jiangxi	Case-control study	31	31	50.00	③㉑㉒	6
Lincheng Sun [24]	2021	Nanyang, Henan	Case-control study	61	237	20.47	①⑬⑯㉑㉒㉗㉜	6
Kun Yang et al. [26]	2020	Nanchong, Sichuan	Case-control study	87	75	34.94	①④⑤⑥⑪⑯㉔㉕㉖㉗㉙㉛	8
Shaobin Yu et al. [29]	2021	Tibet Autonomous Region	cohort study	36	78	31.60	①②⑤⑪⑯㉔㉕㉖㉗㉛㉜㉝	6
Shaobin Yu et al. [27]	2019	Chengdu, Sichuan	cohort study	75	236	24.11	①②④⑤⑪⑲㉑㉔㉖㉗㉜㉝	6

Continued from table 1: Basic information of included studies.

Yan Wang et al. [28]	2021	Hefei, Anhui	cohort study	65	156	29.41	①②⑤⑪⑯㉖㉘㉗㉙ ㉜	6
Li et al. [30]	2021	Kunming, Yunnan	cohort study	49	51	49.00	④⑤⑥⑪⑯⑰㉔㉕㉙	7

Note: ① Age ② History of Diabetes ③ Average Weekly Dialysis Time ④ Serum C-Reactive Protein ⑤ Serum Albumin ⑥ Procalcitonin ⑦ D-Dimer ⑧ Low Shear Apparent Viscosity ⑨ High Shear Apparent Viscosity ⑩ Urea Reduction Rate ⑪ Hemoglobin ⑫ Heart Function Classification ⑬ End-Stage Kidney Disease Duration ⑭ Fasting Blood Glucose ⑮ Smoking History ⑯ Body Mass Index ⑰ Initial Glomerular Filtration Rate ⑱ Cardiothoracic Ratio ⑲ Urea Clearance Index ⑳ Nutritional Status Score ㉑ Dialysis Vintage ㉒ Hemodialysis Method ㉔ White Blood Cell Count ㉕ Platelet Count ㉖ Serum Creatinine ㉗Gender ㉘Concurrent Heart Failure ㉙Neutrophils ㉚Plasma Viscosity ㉛Cholesterol ㉜History of Hypertension ㉝Blood Urea Nitrogen

3.3. Analysis Results of Pulmonary Infection Rate in Patients Undergoing Maintenance Hemodialysis with End-Stage Renal Disease

A total of 21 included studies were subjected to heterogeneity testing and publication bias detection for the pulmonary infection rate in ESRD MHD patients. The results indicated an I^2 of 95%, suggesting significant heterogeneity, leading to selecting a random effects model. The pulmonary infection rate was 37% (95% CI: 23% ~ 60%, *P*<0.01); see Figure 2.

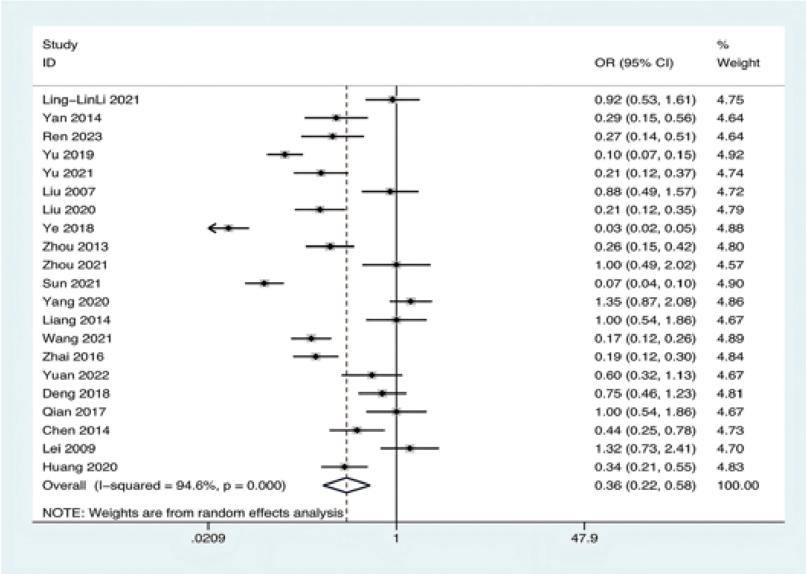

Figure 2: Forest plot of lung infection rates in maintenance hemodialysis patients with end-stage renal disease.

Table 2: Results of meta-analysis of factors influencing lung infection in ESRD maintenance haemodialysis patients

Exposure Factors		Number of Included Studies	Patients (Cases)	Heterogeneity Test		Effect Model	Meta-analysis Result		
				I^2	*P*-value		OR/MD Value	95%CI	*P*-value
Personal Factors	Age	13	659	71	<0.001	Random	7.18	4.61～9.76	<0.001
	Gender	11	778	91	<0.001	Random	0.98	0.52～1.86	0.95
	BMI	7	375	27	0.22	Fixed	-1.01	-1.41～-0.62	<0.001
Past Medical History	Diabetes History	7	354	45	0.09	Fixed	2.83	2.12～3.79	<0.001
	Smoking History	3	132	83	0.003	Random	1.80	0.59～5.49	0.30
	Hypertension History	4	253	0	0.47	Fixed	1.07	0.78～1.47	0.68
Laboratory Tests	CRP	4	160	31	0.23	Fixed	35.46	32.73～38.19	<0.001
	ALB	14	692	92	<0.001	Random	-6.52	-8.68～-4.35	<0.001
	HGB	14	696	97	<0.001	Random	-16.22	-21.35～-11.09	<0.001
	eGFR	2	136	0	0.64	Fixed	0.29	-0.44～1.02	0.43
	URR	3	128	0	0.96	Fixed	-4.48	-5.51～-3.46	<0.001

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	KT/V	10	459	97	<0.001	Random	-0.13	-0.26～0.01	0.05
	WBC	4	247	86	<0.001	Random	2.13	0.90～3.36	0.0007
	PLT	3	172	59	0.09	Random	6.30	-18.72～31.32	0.62
	SCR	6	357	85	<0.001	Random	-32.09	-111.11～46.93	0.43
	NEU	2	114	85	0.009	Random	2.30	-1.57～6.17	0.24
	CH	2	123	40	0.2	Fixed	-0.24	-0.53～0.04	0.09
	BUN	3	163	68	0.05	Random	-0.63	-3.03～1.77	0.61

Continued from table 2: Results of meta-analysis of factors influencing lung infection in ESRD maintenance haemodialysis patients

Laboratory Tests	Cardiothoracic Ratio	4	184	0	0.73	Fixed	0.14	0.13～0.15	<0.001
Other Factors	Course of Disease	2	96	95	<0.001	Random	1.90	0.38～3.43	0.01
	Dialysis Vintage	2	106	38	0.2	Fixed	3.04	2.02～4.06	<0.001
	Average Weekly Dialysis Time	6	269	0	0.46	Fixed	4.53	4.09～4.97	<0.001
	Hemodialysis Method (Conventional Hemodialysis)	2	57	0	0.58	Fixed	2.68	1.6～4.48	0.0002

Notes: CRP: C-reactive protein; ALB: Serum albumin; HGB: Hemoglobin; eGFR: Estimated glomerular filtration rate; URR: Urea reduction ratio; KT/V: Urea clearance index; WBC: White blood cell count; PLT: Platelet count; SCR: Serum creatinine; NEU: Neutrophils; CH: Cholesterol; BUN: Blood urea nitrogen.

3.4. Characteristic Description Results of Patients Undergoing Maintenance Hemodialysis for End-Stage Renal Disease

A meta-analysis of 21 articles was conducted to analyze the characteristics of the study population. The study included patients with ESRD undergoing maintenance hemodialysis (MHD), all of whom had been on regular dialysis for at least three months. Among the included articles, 13 articles [11, 16-22, 25-29] provided a detailed analysis of the age variable, showing that the age range for patients with pulmonary infections was between 40 and 75 years old, with an average age higher than that of patients without pulmonary infections. There were 11 articles [10, 13-14, 18-19, 22, 24, 26-29] that addressed the gender variable, indicating that the number of males and females in the pulmonary infection group and the non-pulmonary infection group of ESRD MHD patients was comparable, with little difference. Upon careful review of the included studies, seven articles [18, 21-22, 26, 28-30] investigated the Body Mass Index (BMI), and the analysis revealed that the BMI of patients in the pulmonary infection group was lower than that of the non-pulmonary infection group. Chronic kidney disease patients often have multiple comorbidities; hemodialysis patients with pulmonary infections commonly have comorbid diabetes and hypertension, and these patients often have a history of smoking. During the data extraction process, fewer articles studied variables such as dialysis vintage, duration of kidney disease, average weekly dialysis time, dialysis method, and dialysis frequency. Patients in the pulmonary infection group undergoing maintenance hemodialysis had a more extended dialysis vintage and kidney disease duration than the non-pulmonary infection group. Based on a dialysis frequency of about four hours per session, 3 to 4 times per week, the average weekly dialysis time for the pulmonary infection group was also higher than that of the non-pulmonary infection group. Additionally, only two articles [23, 24] studied the hemodialysis

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methods for this population. In their research, the dialysis methods for ESRD MHD patients were typically divided into three types: conventional hemodialysis (HD), high-flux hemodialysis (HFD), and hemodialysis combined with hemoperfusion (HP), and most nephropathy patients would choose conventional hemodialysis under actual conditions that allow it.

3.5. Risk Factors for Pulmonary Infections in Patients Undergoing Maintenance Hemodialysis for End-Stage Renal Disease

3.5.1. Personal Factors

A total of 13 articles [11, 16-22, 25-29], including 659 cases of ESRD MHD patients, were subjected to meta-analysis for the age factor. All patients were adults, with I^2 = 71% indicating high heterogeneity between studies, and a random effects model was used. The results showed that the average age of the pulmonary infection group was higher than that of the non-pulmonary infection group [OR = 7.18, 95%CI (4.61 ~ 9.76), *P* value < 0.001], indicating that the older the age, the greater the risk of pulmonary infection in ESRD MHD patients, and advanced age is a risk factor for the development of pulmonary infection in ESRD MHD patients. Eleven studies [10, 13-14, 18-19, 22, 24, 26-29] involving 2449 male ESRD MHD patients were included to explore the gender (male) factor, among which 355 male patients had pulmonary infections. The meta-analysis result showed no significant statistical difference [OR = 0.98, 95%CI (0.52 ~ 1.86), *P* value = 0.98 > 0.05]. For the BMI analysis of 375 ESRD MHD patients from 7 included articles [18, 21-22, 26, 28-30], the World Health Organization (WHO) recommended standard of BMI=weight (kg) / height^2 (m^2) was used [31]. The results indicated that I^2 = 27% with low heterogeneity between studies, and a fixed effects model was applied. The pulmonary infection group had a lower body mass index than the non-pulmonary infection group [OR = -1.01, 95%CI (-1.41 ~ -0.62), *P* value < 0.001], see Table 2.

3.5.2. Past Medical History

Seven articles exploring the association with diabetes history were included [11, 13, 16, 22, 27-19], totaling 1287 ESRD MHD patients, of which 127 patients were in the pulmonary infection group, and 194 patients were in the non-pulmonary infection group. The statistical analysis results showed that I^2=45%, indicating low heterogeneity between studies, and a fixed effects model was used. The pulmonary infection rate in diabetic ESRD MHD patients was higher than in non-diabetic patients [OR=2.83, 95%CI (2.12 ~ 3.79), *P* value < 0.001]. Three articles on smoking history [OR = 1.80, 95%CI (0.59 ~ 5.49, *P* value = 0.30 > 0.05] and four articles on patient hypertension history [OR=1.07, 95%CI (0.78 ~ 1.47, *P* value = 0.68 > 0.05] were separately subjected to meta-analysis, and both results showed no significant statistical differences.

3.5.3. Laboratory Test Results

A total of 4 studies [12, 17, 20, 25], including 160 cases of ESRD MHD patients with pulmonary infection, were included to study CRP, with I^2 = 31% indicating low heterogeneity between studies, and a fixed effects model was used. The results showed that the CRP level in the pulmonary infection group was higher than in the non-pulmonary infection group [OR = 35.46, 95%CI (32.73 ~ 38.19), *P* value < 0.001]. Fourteen studies were included to analyze the ALB factor [11-12, 16-17, 19-22, 25-30] and HGB factor [11, 16-18, 20-22, 25, 26-30], involving 692 samples for ALB levels and 696 samples for HGB levels. Both results indicated that the levels of ALB and HGB in the pulmonary infection group were lower than in the non-pulmonary infection group [OR = -6.52, 95%CI (-8.68 ~ -4.35), *P* value < 0.001; OR = -16.22, 95%CI (-21.35 ~ -11.09), *P* value < 0.001]. By using URR and KT/V in combination to study the adequacy of dialysis, 3 URR articles [11-12, 16], including 128 cases of ESRD MHD patients with pulmonary infection, and 10 KT/V articles [11-12, 16-18, 20-22, 25, 27] including 459 cases of ESRD MHD patients with pulmonary infection were included in the meta-analysis. The results showed that the levels of URR and KT/V in the pulmonary infection group were lower than in the non-pulmonary infection group [OR = -4.48, 95%CI (-5.51 ~ -3.46), *P* value < 0.001; OR = -0.13, 95%CI (-0.26 ~ 0.01), *P* value = 0.05]. The more adequate the dialysis, the better the dialysis effect, and the lower the risk of pulmonary infection in ESRD MHD patients. A total of 4 articles [26-27, 29-30], including 247 cases of ESRD MHD patients with pulmonary infection, were included to study the WBC factor, with I^2=86% indicating high heterogeneity between studies, and a random effects model was used. The results showed that the white blood cell count level in the pulmonary infection group was higher than in the non-pulmonary infection group [OR = 2.13, 95%CI (0.90 ~ 3.36), *P* value < 0.001]. A total of 4 articles [18, 21-22, 25], including 184 cases of ESRD MHD patients, were included to perform a meta-analysis of the cardiothoracic ratio index, with I^2=0%

indicating low heterogeneity between studies, and a fixed effects model was used. The results showed that the cardiothoracic ratio in the pulmonary infection group was higher than in the non-pulmonary infection group [OR = 0.14, 95%CI (0.13 ~ 0.15), *P* value < 0.001]. For eGFR [OR = 0.29, 95%CI (0.44 ~ 1.02), *P* value = 0.43], PLT [OR = 6.30, 95%CI (-18.72 ~ 31.32), *P* value = 0.62], SCR [OR = -32.09, 95%CI (111.11 ~ 46.93), *P* value = 0.43], NEU [OR = 2.30, 95%CI (-1.57 ~ 6.17), *P* value = 0.24], CH [OR = -0.24, 95%CI (-0.53 ~ 0.04), *P* value = 0.09], BUN [OR = -0.63, 95%CI (-3.03 ~ 1.77), *P* value = 0.61], there were no statistical differences between the pulmonary infection group and the non-pulmonary infection group.

3.5.4. Other Factors

A meta-analysis was conducted on chronic renal failure as a factor in two studies, one by Huang Ningchuan et al. [19] and the other by Liu Pei et al. [12], involving 96 patients with pulmonary infection. The results indicated high heterogeneity between studies with $I^2 = 95\%$, and a random effects model was used. The average course of disease in the pulmonary infection group was longer than in the non-pulmonary infection group [OR = 1.90, 95%CI (0.38 ~ 3.43), *P* value < 0.001], indicating that the course of disease is a high-risk factor for pulmonary infection in ESRD MHD patients. The average weekly dialysis time was analyzed in 6 studies [18-19, 21-23, 25] involving 269 ESRD MHD patients with pulmonary infection, with low heterogeneity between studies at $I^2 = 0\%$, and a fixed effects model was used. The results showed that the average weekly dialysis time in the pulmonary infection group was significantly longer than in the non-pulmonary infection group [OR = 4.53, 95%CI (4.09 ~ 4.97), *P* value < 0.001]. Two studies [23, 27] involving 373 ESRD MHD patients were included to compare dialysis vintage as a factor, which included 106 patients with pulmonary infection and 267 without. With low heterogeneity between studies at $I^2 = 38\%$, a fixed effects model was used. The results indicated that the dialysis vintage in the pulmonary infection group was significantly longer than in the non-pulmonary infection group [OR = 3.04, 95%CI (2.02 ~ 4.06), *P* value < 0.001], with a significant statistical difference between the groups. To understand the impact of hemodialysis methods on ESRD MHD patients with pulmonary infection, two studies [23-24] were included to assess the effect on 57 ESRD MHD patients with pulmonary infection. The results showed a significant statistical difference between the pulmonary infection group and the non-pulmonary infection group [OR = 2.68, 95%CI (1.6 ~ 4.48), *P* value < 0.001], indicating that the method of hemodialysis is related to the occurrence of pulmonary infection in ESRD MHD patients.

3.6. The Isolation Rate of Infectious Flora in Patients with End-Stage Renal Disease Undergoing Maintenance Hemodialysis with Pulmonary Infection

An analysis was conducted using seven articles [12, 16-18, 21-23] that detailed the infectious flora, with 285 specimens submitted for testing. A total of 155 positive bacterial cultures were identified, all sputum cultures, resulting in a bacterial culture rate of 89%. The main isolated strains were Gram-negative bacteria, with a total of 97 strains, accounting for an isolation rate of 34%, followed by Gram-positive bacteria, with a total of 75 strains, accounting for an isolation rate of 26%. The literature analysis concluded that bacterial infections are the leading infectious flora in patients with ESRD undergoing maintenance hemodialysis who have pulmonary infections. The top 3 most common Gram-negative bacteria that cause pulmonary infection are Klebsiella pneumoniae, Pseudomonas aeruginosa, and Haemophilus influenzae.

3.7. Publication Bias Situation

Meta-analysis was conducted on the correlation between age, ALB (albumin), HGB (hemoglobin), KT/V (urea clearance index), and pulmonary infection, with more than ten articles included and all having statistical significance, while gender had no statistical significance. The Rev Man 5.4 software was used to draw the funnel plot, and the Stata15.0 software was used to draw Begg's plot to detect publication bias for the studies included with the above five statistically significant factors. The funnel plot is shown in Figure 3, and the results indicate that age, HGB, and KT/V are relatively stable. The Begg’s test results further confirmed that age (*P* value = 0.36), HGB (*P* value = 0.324), and KT/V (*P* value = 1) all had no statistical significance, meaning there was no publication bias, and the results were reliable. However, the pulmonary infection rate (*P* value = 0.025) and ALB (*P* value = 0.029) had statistical significance, indicating the presence of some publication bias, as seen in Figure 4.

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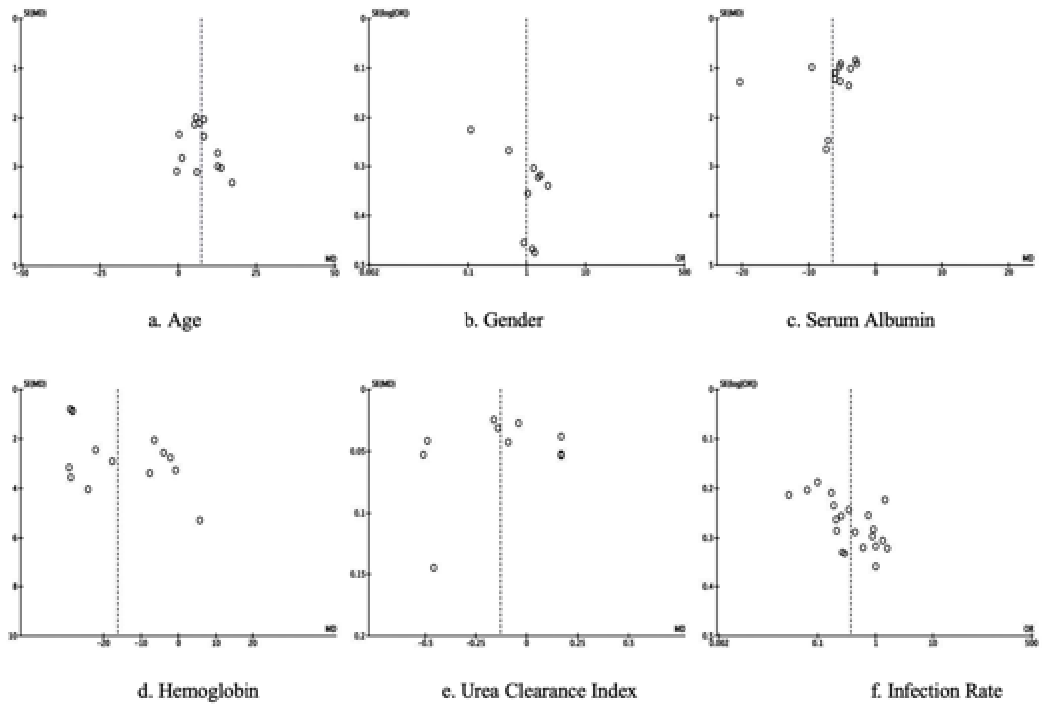

Figure 3: Funnel plot of factors influencing lung infection in maintenance hemodialysis patients with end-stage renal disease

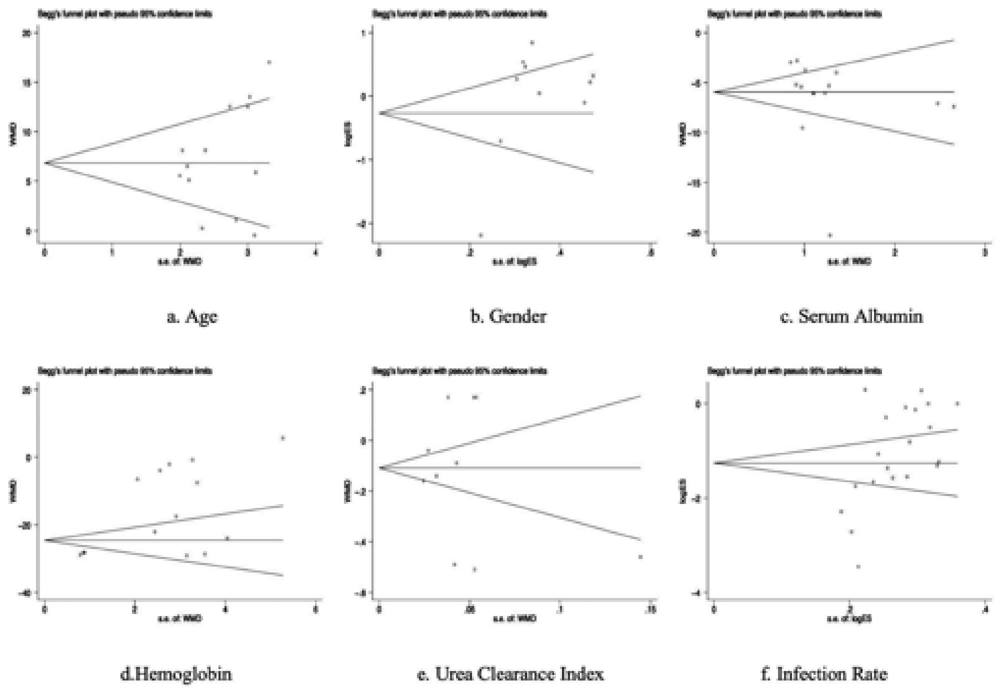

Figure 4: Begg's test plot of factors influencing lung infection in maintenance haemodialysis patients with end-stage renal disease.

3.8. Heterogeneity and Sensitivity Analysis

Sensitivity analysis was conducted on the meta-analysis results with heterogeneity $I^2 \geq 50\%$ [8]. The analysis indicated that age, gender, smoking history, PLT (platelet count), SCR (serum creatinine), ALB (albumin), HGB (hemoglobin), WBC (white blood cell count), disease course factors, and pulmonary infection rates had low sensitivity, with statistical analysis results being relatively stable and reliable. However, sensitivity analysis results for URR (urea reduction ratio), KT/V (urea clearance index), NEU

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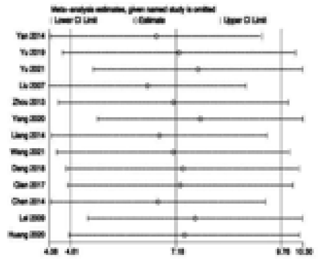
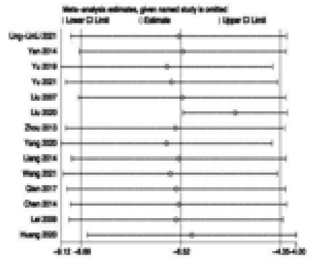
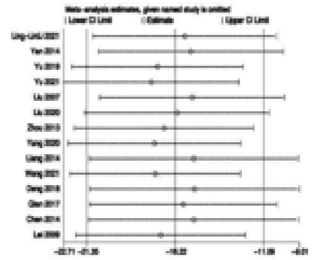
(neutrophils), and BUN (blood urea nitrogen) showed significant fluctuations, demonstrating notable heterogeneity. See Figure 5.



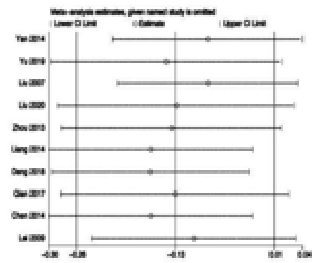
a. Age



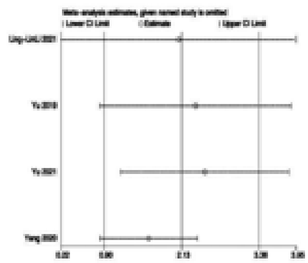
b. Albumin



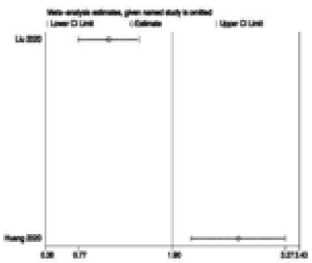
c. Hemoglobin



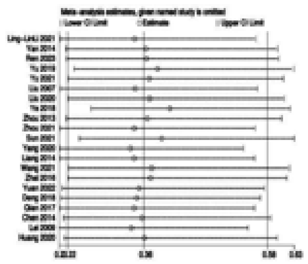
d. Urea Clearance Index



e. White Blood Cell Count



f. Disease Course



g. Disease Course

Figure 5: Sensitivity analysis of factors influencing lung infection in maintenance hemodialysis patients with end-stage renal disease.

4. Discussion

4.1. Risk of Pulmonary Infection in Patients with Renal Failure and Countermeasures

Pulmonary infection is one of the common complications in patients with End-Stage Renal Disease (ESRD) undergoing Maintenance Hemodialysis (MHD), with a high incidence rate and potentially severe consequences. This study examined 21 relevant articles to explore these patients' risk factors for pulmonary infection. Our research analyzed personal factors, past medical history, laboratory test results, and other factors involved in the risk factors. The study included cases from different periods, regions, and hospitals, where the sanitary environment and medical conditions varied, and the analysis of some factors was based on only two or three articles, which may affect the heterogeneity between studies. Patients with chronic renal failure are prone to adverse infectious events because uremia is associated with changes in the primary host defense mechanisms. Neutrophils in hemodialysis patients have impaired functions such as chemotaxis, oxidative metabolism, phagocytosis, degranulation, intracellular killing, and programmed cell death [32], increasing the risk of bacterial infection, with pneumonia being a common and significant bacterial infection of the pulmonary parenchyma, particularly evident in ESRD MHD patients [33]. The results of this meta-analysis show that pulmonary infection is the outcome of the combined action of multiple factors, with infection rates varying from 15.1% to 50%, consistent with

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existing studies [34], which may be due to sample size, study type, and region. Once pulmonary infection occurs, it can lead to disease deterioration and accelerate the progression of ESRD MHD patients. When pulmonary infection is present, microbiological smear tests and bacterial culture identification should be carried out promptly to detect pathogens early, select sensitive antimicrobial drugs targeted, provide treatment plans, and thus improve patient survival rates and outcomes. Patients with renal failure often have impaired immune function due to the reduced detoxification capability of the kidneys and the accumulation of metabolic waste, increasing their susceptibility to pulmonary infections. These patients are not only at a higher risk of infection due to the potential catheter infection risks during the dialysis process, but their underlying diseases, such as diabetes and cardiovascular diseases, also contribute to the occurrence of infections. Therefore, developing targeted preventive measures, including regular pulmonary health monitoring, vaccination against influenza and pneumonia, maintaining good personal hygiene habits, and a balanced diet to enhance immune system function is essential. In addition, patients should be encouraged to exercise moderately and, under the guidance of professional medical staff, control their underlying diseases to reduce the risk of pulmonary infection and improve the overall prognosis of patients.

4.2. The Impact of Advanced Age and Gender on Pulmonary Infection in Patients Undergoing Maintenance Hemodialysis

Consistent with our research findings, a previous study [13] also found that advanced age is one of the critical risk factors for developing pulmonary infection in patients undergoing maintenance hemodialysis. With increasing age, coupled with the gradual decline in immune system function due to long-term dialysis, the elasticity of alveoli decreases, and the permeability of the respiratory tract increases, which allows pathogens to invade more easily and weakens the protective function of mucosal barriers, thereby increasing the risk of infection [35-36]. Our study demonstrates that gender has no significant impact on the occurrence of pulmonary infection in ESRD MHD patients, which is in line with previous research.

4.3. The Association between Nutritional Indicators and the Risk of Pulmonary Infection in Patients with End-Stage Renal Disease

Nutritional indicators also play a significant role in patients with end-stage renal disease (ESRD). Malnutrition is an essential factor affecting patients' immune functions. In this state, patients are in a negative nitrogen balance, leading to increased consumption of protein and muscle, thereby reducing immunity and the body's resistance to pathogens, increasing the risk of infection [19]. Our study concludes that malnutrition is closely related to the occurrence of pulmonary infection, and the decline in levels of albumin (ALB), hemoglobin (HGB), and body mass index (BMI) is significantly correlated with an increased risk of pulmonary infection. ALB is an essential factor in regulating the immune system, helping the body fight infections. In patients with pulmonary infection, the level of ALB is often affected, and hypoalbuminemia may lead to decreased immune function, increasing the risk of infection [37]. Patients with chronic kidney disease usually experience renal anemia, with a reduction in HGB. Anemia can lead to decreased oxygen transport capacity, affecting oxygenation in the lungs and throughout the body [38]. In the case of pulmonary infection, adequate HGB levels are significant for maintaining oxygenation function. On the one hand, patients with lower BMI may be at risk of malnutrition and decreased immune function, increasing their likelihood of developing pulmonary infection [39], which is consistent with our research. On the other hand, patients with higher BMI may have immune function abnormalities related to obesity, which may also increase the risk of infection. Therefore, hemodialysis patients should monitor their hemoglobin levels regularly and receive anemia treatment according to medical advice, such as iron supplementation or erythropoietin therapy. At the same time, they should control their weight according to medical advice, maintain an appropriate body mass index, and also keep adequate albumin levels by consuming protein-rich foods or receiving albumin transfusions to maintain good nutritional status and enhance immune function to prevent infections.

4.4. The Impact of Relevant Past Medical History on Pulmonary Infection in Patients with End-Stage Renal Disease

In our study, a history of diabetes mellitus is a risk factor for pulmonary infection in ESRD MHD patients. Patients with diabetes are more susceptible to opportunistic infections due to impaired antioxidant defense mechanisms in the lungs. Additionally, a hyperglycemic environment provides an ideal condition for the growth and proliferation of bacteria and other pathogens [40]. Hyperglycemia weakens the function of white blood cells, making it difficult for them to clear pathogens, which increases the risk of infection effectively. Long-term hyperglycemia can lead to microvascular changes in the lungs, causing lung tissue hypoxia, reducing the pulmonary capillary bed, and decreasing lung surface-active substances, increasing the risk of pulmonary infection [41]. We have demonstrated that a history of hypertension and smoking history have little impact on the acquisition of pulmonary infection in ESRD MHD patients. Hypertension is usually related to the cardiovascular system, while pulmonary infection is mainly related to the respiratory system. Furthermore, the treatment of hypertension typically involves controlling blood pressure and reducing the risk of cardiovascular diseases rather than directly affecting the function of the immune or respiratory systems. Hypertension does not have a direct impact on pulmonary infection. The study on smoking history included only three articles, which may affect the research results.

4.5. Inflammatory Markers of Pulmonary Infection in Patients with End-Stage Renal Disease

The meta-analysis results suggest that CRP (C-reactive protein) and WBC (white blood cell) counts are inflammatory markers for pulmonary infection in patients undergoing maintenance hemodialysis. CRP is an acute-phase protein that increases rapidly in response to inflammation or infection. CRP levels can be an essential biomarker for monitoring inflammatory status and infection in dialysis patients. In cases of concurrent pulmonary infection, CRP levels usually rise significantly, reflecting the body's inflammatory response. During treatment, the dynamic monitoring of CRP can also help assess the effectiveness of the treatment and guide adjustments to the therapeutic plan. Additionally, we analyzed whether an increase in WBC counts could increase the risk of pulmonary infection, and the results indicate that WBC can be one of the inflammatory markers for pulmonary infection in ESRD MHD patients. White blood cells are one of the primary cells in the body's immune system, responsible for fighting infections. When the body is infected, white blood cells increase rapidly to combat the invasion of pathogens. When hemodialysis patients have pulmonary infections, the inflammatory response triggered by the pathogens causes an increase in white blood cell counts to enhance immune cells' fight against the infection. Maintaining good personal hygiene habits, such as frequent handwashing, dressing appropriately, and ensuring good indoor air circulation, can reduce the chances of bacteria and viruses entering the respiratory tract.

4.6. The Clinical Significance of the Cardiothoracic Ratio Index and Dialysis Adequacy in Patients with End-Stage Renal Disease

Literature has shown [42] that cardiovascular diseases are one of the common complications in patients with ESRD, especially those undergoing hemodialysis treatment. In our study, we analyzed the impact of the cardiothoracic ratio index on the occurrence of pulmonary infection in patients with end-stage renal disease. We found that this level is a risk factor for pulmonary infection. This may be because cardiac enlargement leads to reduced cardiac function, affecting the heart's pumping function, thereby affecting pulmonary circulation and increasing the risk of pulmonary infection. Additionally, cardiac enlargement may also affect the operation of respiratory mechanics, weakening ventilation function and making the lungs more susceptible to infection. Furthermore, we combined KT/V, URR, the course of nephropathy, dialysis vintage, weekly dialysis time, and the method of hemodialysis to study the impact of dialysis adequacy on the occurrence of pulmonary infection in ESRD MHD patients from multiple aspects. The meta-analysis concluded that inadequate dialysis increases the risk of pulmonary infection. Although some indicators were studied with only 2-3 articles, they still have specific clinical implications. During the hemodialysis process, if dialysis adequacy is insufficient, the waste and toxins in the patient's body cannot be effectively removed, leading to the accumulation of toxins in the body and affecting the function of the immune system. A decline in immune system function makes patients more susceptible to infections. Moreover, inadequate dialysis adequacy may lead to malnutrition and a decline in immunity in patients, thereby increasing the risk of infection. In clinical practice, for such high-risk groups, there should be increased monitoring and preventive measures for pulmonary infection. Some foreign studies have pointed out [43] that one prevention method is to recommend vaccination for all ESRD patients and to revaccinate after 5 years while avoiding cross-infection. In addition, future research can further explore the potential mechanisms between these risk factors and pulmonary infection to better guide clinical practice.

5. Limitations

This study has certain limitations. On one hand, most of the literature included in this study were

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retrospective studies, which limits the credibility of the research conclusions. In future work, more prospective cohort and cross-sectional studies should be conducted to more accurately and objectively assess the infection rates and risk factors for pulmonary infection in patients with end-stage renal disease undergoing maintenance hemodialysis. On the other hand, some influencing factors were analyzed with only 2-3 articles in the meta-analysis, which may interfere with the analysis results. Subsequent studies require more high-quality research to verify these findings.

6. Summary

In summary, age, body mass index, history of diabetes, C-reactive protein, serum albumin, hemoglobin, urea clearance index, white blood cell count, cardiothoracic ratio, course of nephropathy, dialysis vintage, average weekly dialysis time, and hemodialysis method are all independent risk factors for pulmonary infection in patients with end-stage renal disease undergoing maintenance hemodialysis. It is necessary to promptly assess the risk factors for pulmonary infection in patients and take targeted measures to prevent infection in order to improve patient outcomes.

Data availability statement

The original contribution of this study is presented in detail in the article; for further information, please contact the corresponding author directly.

Author contributions

FL: Data curation, Formal analysis, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. CH H: Formal analysis, Methodology, Project administration, Supervision, Validation, Writing – original draft, Writing – review & editing. HL: Formal analysis, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. XL: Project administration, Supervision, Validation, Writing – review and editing.

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