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Translating Mesenchymal Stem Cell Research into Chronic Kidney Disease Therapy: A Systematic and Clinical Review

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ABSTRACT

Chronic kidney disease (CKD) is a progressive disorder with high morbimortality and limited treatment options. Mesenchymal stem cells (MSCs) have emerged as a promising therapy because of their immunomodulatory and regenerative properties. This systematic review evaluates the therapeutic potential of MSC therapy for CKD by searching databases PubMed, Medline, Embase, the Cochrane Library, and Scopus from January 2000 to May 2026 using keywords “mesenchymal stem cells,” “cell therapy,” and “renal failure”. Among 1,525 identified studies, 19 met the inclusion criteria, covering preclinical and clinical investigations. Findings indicated contribution of MSC therapy to renal tissue repair, immunomodulation, and functional recovery, with some studies reporting improvements in glomerular filtration rate, reduced proteinuria, and histological recovery of kidney tissue. While the short-term safety profiles were favorable, the long-term efficacy and optimal administration protocols remain uncertain. Further high-quality clinical trials are needed to establish standardized treatment protocols and validate long-term benefits.
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Keywords: Chronic kidney disease, Mesenchymal stem cells, Renal insufficiency

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1. INTRODUCTION

Chronic kidney disease (CKD) is a progressive condition characterized by a gradual loss of kidney function and structure, affecting a significant portion of the global population (Fig.1)[1]. Common causes of CKD include inflammation, aging, hypertension, and diabetes. Despite advancements in management through medications and renal replacement therapies, CKD remains a significant public health concern due to its numerous complications and substantial disease burden[2]. Patients in the advanced stages of CKD often exhibit common manifestations such as glomerulosclerosis, vascular sclerosis, and tubulointerstitial fibrosis, suggesting a shared final pathway of progressive injury involving processes like apoptosis, oxidative damage, and microvascular rarefaction[3,4].

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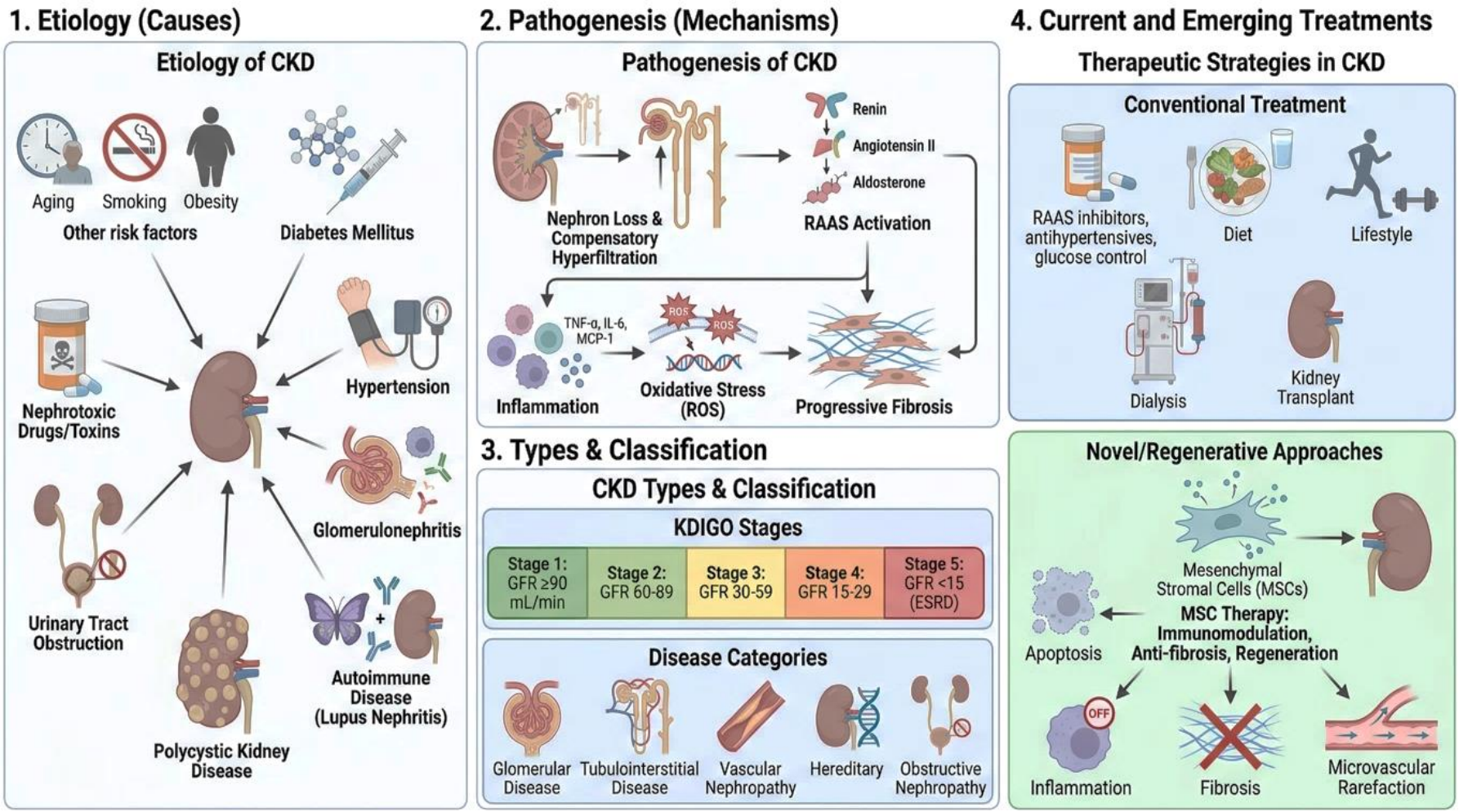

Fig. 1. Schematic overview of CKD, detailing its etiology, pathogenesis, types, and therapeutic strategies. The Figure illustrates the main causes of CKD, including diabetes, hypertension, autoimmune disorders, and nephrotoxic injury. The diagram also shows key pathogenic mechanisms such as inflammation, oxidative stress, fibrosis, and nephron loss, leading to progressive renal dysfunction and end-stage renal disease (created by FigureLabs.ai).

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Various cellular and molecular pathways—including the activation of mesangial cells and fibroblasts, renin-angiotensin-aldosterone system, production of cytokines and growth factors, epithelial-mesenchymal transition, and immune cell infiltration—contribute to the progression of kidney damage in CKD[5,6]. While the kidney possesses some regenerative capacity that allows for organ recovery, this ability is often limited and insufficient to prevent fibrosis. CKD can ultimately progress to end-stage renal disease, underscoring the need for novel therapies to halt or slow down the kidney damage process[7]. Stem cell transplantation, particularly utilizing mesenchymal stem cells (MSCs), has shown promise in both preclinical and clinical settings for CKD treatment[8,9]. MSCs are adult stem cells of mesodermal origin that exhibit regenerative and paracrine properties[10]. These cells release proteins and hormones that can impact pathways like apoptosis, fibrosis, inflammation, and microvascular rarefaction[11,12]. These characteristics render MSCs a suitable option for addressing CKD[13].

This review paper provides an overview of the clinical applications of various types of MSCs in different types of CKD. By comparing the efficacy and outcomes of using different MSCs in CKD therapy, we have gained valuable insights into the potential benefits and limitations of each MSC type. The findings highlight the promising role of MSC-based therapies in the management of CKD and underscore the need for further research to optimize treatment strategies and improve patient outcomes. As we continue to bridge the gap between laboratory research and clinical practice, using MSCs for therapy shows great potential in improving CKD treatment and helping patients.

2. SEARCH STRATEGY AND STUDY SELECTION

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive literature search was performed in PubMed/MEDLINE, Embase, Scopus, and the Cochrane Library from database inception from January 2000 to May 2026, to identify studies evaluating MSC-based therapies in renal diseases. The search strategy combined Medical Subject Headings (MeSH) terms and free-text keywords related to MSC therapy and renal disorders. The primary search terms included “Mesenchymal Stem Cells”, “Mesenchymal Stromal Cells”, “Stem Cell Therapy”, “Cell Therapy”, “Chronic Kidney Disease”, “Kidney Failure, Chronic”, “Renal Failure”, “Acute Kidney Injury”, “Diabetic Nephropathy”, “Lupus Nephritis”, and “Kidney Transplantation.” Boolean operators (AND and OR) were applied to appropriately combine the search terms. An example of the PubMed search strategy was as follows: (“Mesenchymal Stem Cells” [Mesh] OR “mesenchymal stem cells” OR MSCs OR “mesenchymal stromal cells”) AND (“Kidney Failure, Chronic” [Mesh] OR “chronic kidney disease” OR CKD OR “renal failure” OR “acute kidney injury” OR AKI. The search syntax was adapted according to the requirements of each database. In addition, the reference lists of eligible articles were manually screened to identify potentially relevant studies not captured in the initial database search. Clinical trial registries, including ClinicalTrials.gov, were also searched to identify ongoing or recently completed clinical trials investigating MSC therapy in kidney diseases.

Studies included in this review had to be clinical studies, including randomized and non-randomized trials, pilot studies, and case reports, investigating MSC-based therapy in the patients with kidney diseases or renal failure. Eligible studies involved human participants and reported therapeutic efficacy, safety outcomes, renal functional parameters, or adverse events associated with MSC administration. Only peer-reviewed articles published in English were considered for inclusion. Animal studies, in vitro experiments, review articles, conference abstracts, editorials, expert opinions, and book chapters were excluded. Studies lacking adequate MSC characterization or a clearly described administration protocol, as well as studies unrelated to renal diseases or kidney dysfunction, were also excluded. Two independent reviewers screened all retrieved records based on titles and abstracts. Full-text articles were subsequently assessed for eligibility when sufficient information was unavailable in the abstract or when relevance was uncertain. Any disagreements between reviewers were resolved through discussion and consensus, with a third reviewer involved when necessary. Relevant data were independently extracted by two reviewers using a structured Excel spreadsheet. The extracted variables consisted of first author and year of publication, study design and clinical trial phase, MSC source and type, route of administration, MSC dose and treatment frequency, number of enrolled patients, type of renal disease, primary clinical and laboratory outcomes, follow-up duration, and adverse events or safety outcomes. Any discrepancies in data extraction were resolved through reviewer consensus prior to final analysis.

3. RESULTS

A total of 1525 articles were identified through database searches. After removing duplicates (992 articles), 533 studies remained for screening. Based on a review of the titles and abstracts, 453 studies were excluded for not meeting the inclusion criteria. In total, 80 full-text articles were assessed for eligibility, of

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which 61 were excluded due to reasons such as being preclinical studies, lacking MSC characterization, or reporting insufficient outcomes. Finally, 19 studies met the inclusion criteria and were included in the systematic review. The PRISMA flowchart summarizing the study selection process is presented in Figure 2.

3.1. Application of MSCs in kidney transplantation

While MSC-based therapies in kidney transplantation were considered in this review, greater emphasis was placed on CKD and acute kidney injury (AKI), as these conditions represented the primary focus of the current analysis. Accordingly, transplantation-related studies are discussed more concisely. MSCs have attracted significant interest in the field of kidney transplantation due to their unique immunomodulatory and regenerative properties. Clinical studies investigating the use of MSCs in kidney transplant recipients have shown promising results, suggesting that MSC therapy may offer a novel approach to improve outcomes in this patient population[14].

The primary objectives of clinical trials exploring the application of MSCs in kidney transplant recipients encompass the prevention of rejection, renal repair and regeneration, reduction of drug toxicity, and enhancement of graft survival. Early clinical studies have shown that MSC therapy is safe and feasible. In a 2011 study by Perico et al., two patients with end-stage renal disease underwent renal transplantation and received autologous MSCs post-transplantation. The infused cells (1.7–2.0 × 10^6 cells/kg body weight) were administered intravenously seven days after the kidney transplant. Although both patients developed renal insufficiency after cell infusion, they were carefully

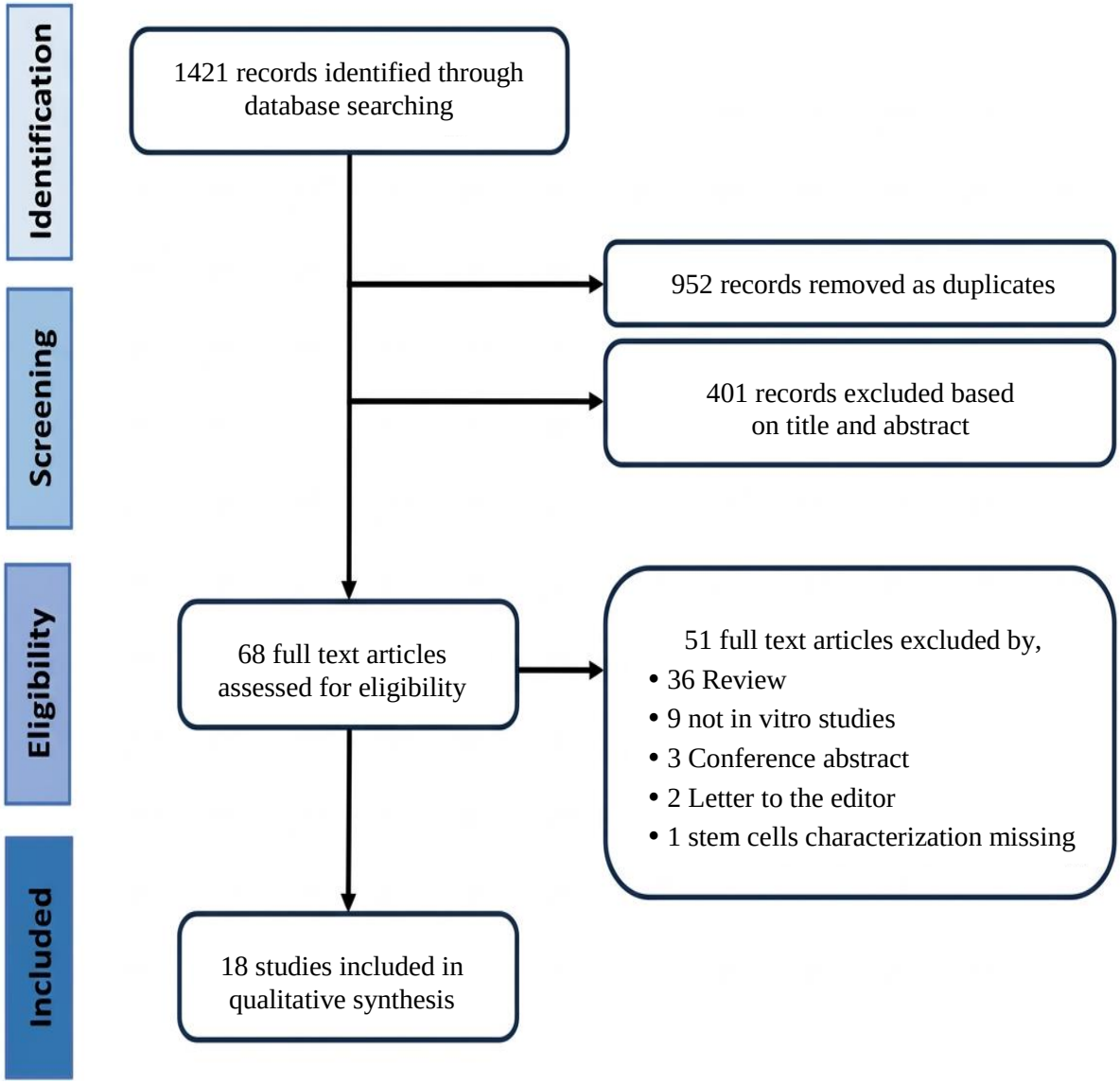

Fig. 2. PRISMA flow diagram of literature search from January 2000 to May 2026.

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monitored, and their graft function was stabilized over time. The study also explored the in vivo effects of MSCs infusion on T-cell homeostasis and post-transplantation function. It was observed that MSCs infusion led to a decrease in memory $CD8^+$ T cells and an increase in regulatory T cells, potentially contributing to a protolerogenic environment. However, further research was imperative to refine the timing and protocol of MSCs infusion to minimize adverse effects and maximize therapeutic benefits in solid organ transplantation settings[15]. In a subsequent study by El-Ansary et al., a dose-dependent approach was adopted to optimize MSC therapy in kidney transplant recipients. Patients were categorized into three groups: those with inactive systemic lupus erythematosus (SLE) and diffuse proliferative lupus nephritis, renal transplantation cases with chronic allograft nephropathy, and a control group with impaired renal function due to other causes. These patients received intravenous (IV) infusions of MSCs at a dose of 50-70 million MSCs in 10 mL saline, administered in two divided doses one week apart. A significant correlation was observed between MSC dose and a decrease in serum creatinine (SCr) levels after injection. Microchimerism research confirmed the persistence of donor MSCs in the renal transplanted group, aiding in the development and maintenance of immunological tolerance. The follow-up of the patients at 1, 3, and 6 months after MSC injection showed higher hemoglobin levels, a reduction in mean SCr, and an elevation in the mean of creatinine clearance levels[16]. A study in 2013 explored the dose-dependency and the interval of administration in post-transplantation, involving six renal transplant recipients with subclinical rejection and interstitial fibrosis/tubular atrophy (IFTA). These patients received two IV doses of $1–2 \times 10^6$ bone marrow (BM)-MSCs per kilogram of body weight, administered seven days apart. Clinical and immunological monitoring was conducted for up to 24 weeks post-MSC infusions. Notably, a downregulation of the mixed lymphocyte reaction to the donor was observed in five out of six patients, indicating an immunomodulatory effect of MSC therapy. Additionally, in the recipients with allograft rejection, renal biopsies post-MSC treatment demonstrated the resolution of tubulitis without IFTA, suggesting that MSCs may help mitigate rejection episodes. Levels of Interferon-γ, interferon-γ-induced protein-10, and monocyte chemoattractant protein (MCP)-1 decreased in the majority of patients upon stimulation with donor-specific peripheral blood mononuclear cells, indicating the potential immunomodulatory effect of MSC treatment. This study provides valuable insights into the potential benefits and immunological effects of MSC therapy in renal transplant recipients[17]. A six-month randomized, double-blind, phase two study investigated the efficacy and safety of combining concentration-controlled everolimus with MSCs, compared to everolimus with standard tacrolimus, in de novo renal recipients. Thirty-five patients received everolimus with MSCs, while another 35 received everolimus with standard tacrolimus. Autologous BM-MSCs were administered at two doses of 1.5×10^6 MSCs per kg body weight at weeks 6 and 7 post-transplantation. This study aimed to explore the potential of MSCs and everolimus in providing a more effective and tolerogenic approach to immunosuppression in transplant recipients. Reinders et al., in 2013, showed promising results in reducing peripheral blood mononuclear cell proliferation and enhancing regulatory T cells with MSC treatment[17]. In 2014, Reinders et al. aimed to conduct meaningful comparisons of immune profiles between MSC-treated and untreated groups to assess the immunomodulatory effects of MSCs[18]. Additionally, the study by the same author explored the potential cardioprotective effects of everolimus and MSCs in reducing the burden of cardiovascular disease post-transplantation[18]. Zhang et al.'s survey in 2021 focused on 11 renal transplant patients with IFTA. Following intra-arterial infusion of BM-MSCs, SCr levels decreased significantly at seven days, one month, and three months compared to baseline, while creatinine clearance increased significantly at these time points. Cystatin-C levels showed a similar trend to SCr. Individual patient analysis revealed that renal function improved in 54.5% of patients, remained stable in 27.3%, and worsened in 18.2% at 12 months post-infusion. Protein expressions of key renal fibrotic factors, such as transforming growth factor beta-1 (TGF-β1) and connective tissue growth factor, significantly decreased following BM-MSC treatment, underlining the therapeutic potential of MSCs in ameliorating renal fibrosis. No severe adverse events were reported during the one-year follow-up. The study underscores the significance of the administration route in achieving positive outcomes, highlighting the potential benefits of intra-arterial delivery of MSCs over IV infusion. Moreover, a specific treatment protocol involving intra-arterial infusion followed by IV infusion was proposed to enhance therapeutic effects (Fig. 3)[19].

3.2. Application of MSCs in CKD

The studies investigating MSC therapy in CKD have demonstrated variable improvements in renal function, inflammatory biomarkers, and proteinuria[20-22]. The immunomodulatory and regenerative properties of MSCs, along with their ability to reprogram inflammatory responses and promote tissue repair, make them a valuable tool in combating the progression of diabetic nephropathy and other forms of CKD[23]. In a

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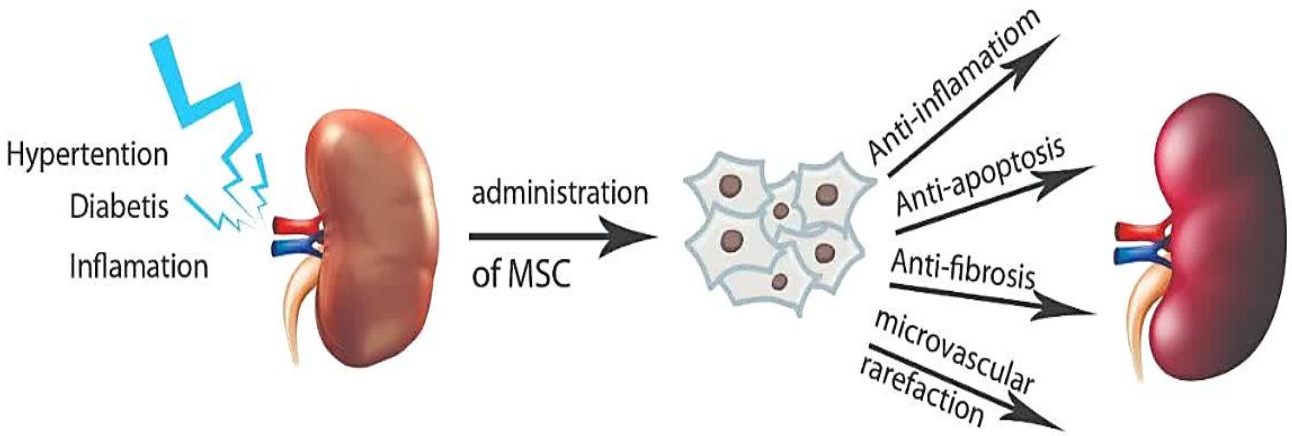

Fig. 3. Potential mechanism of MSCs in improving CKD symptoms.

double-blind, placebo-controlled trial conducted in 2016, 30 patients with CKD due to type 2 diabetes and advanced diabetic nephropathy were treated with an allogeneic, bone marrow-derived mesenchymal lineage cell product (rexlemestrocel-L). The trial administered a single IV infusion of rexlemestrocel-L at two fixed doses (150×10^6 or 300×10^6 cells), which were well-tolerated and exhibited a consistent safety profile across all treatment groups. While the study was not powered to assess efficacy, the primary exploratory efficacy parameter was the effect of rexlemestrocel-L on renal function over 12 weeks. No significant effects were noted for various biomarkers; however, there was a suggestion for stabilization of estimated glomerular filtration rate (eGFR) in the rexlemestrocel-L 150×10^6 cell group compared to placebo at the 12-week endpoint. The lack of changes in glycemic parameters suggests that the observed effects were likely unrelated to changes in diabetes control[24]. Rahyussalim et al. explored the use of human umbilical cord mesenchymal stem cells (hUC-MSCs) in a case study involving a 62-year-old Indonesian woman with thoracic spinal cord entrapment, paraplegia, and chronic renal failure (CRF) requiring hemodialysis. The treatment protocol involved six cycles of hUC-MSC intrathecal implantation and IV injection at three-month intervals. After the second cycle, the patient showed improvement in leg movement, increased sensory level, and the ability to urinate for the first time in two years. Notably, the creatinine level decreased significantly to 2 mg/dl after treatment, indicating improved renal function. This study emphasized the potential of hUC-MSCs in regenerative medicine due to their self-renewal ability and differentiation potential. Compared to BM-MSCs, hUC-MSCs have advantages such as easy acquisition, high proliferation ability, low immunogenicity, and fewer ethical concerns[23].

An open-label, single-arm trial conducted by Makhlough et al. evaluated the safety and tolerability of autologous MSC infusion in seven CKD patients with various known etiologies, including hypertension, nephrotic syndrome, focal segmental glomerulo sclerosis, and also unknown etiology. The study did not demonstrate significant improvements in eGFR or SCr levels following the IV administration of a single dose ($1\text{-}2 \times 10^6$ cells/kg) of autologous MSC infusion in CKD patients. Although the procedure was found to be safe and well-tolerated, the progressive decline in kidney function, indicated by eGFR and SCr levels[22], suggests that the single dose of MSC infusion may not be effective in halting or reversing the course of CKD in these patients, which is consistent with a previous finding[15]. Makhlough et al.'s study had limitations, including a small sample size and the absence of a control group, which affects the ability to draw definitive conclusions on efficacy. However, the main advantage of the study was the longest follow-up period (18 months) trial to assess the safety and tolerability of autologous MSC infusion in CKD patients[22].

In 2021, a randomized controlled trial was conducted in China involving 200 patients diagnosed with CRF with an eGFR below 60 mL per minute per 1.73 m². The trial compared the effects of IV infusion of marrow-derived autologous MSCs at dosages ranging from 1×10^6 to 2×10^6/kg with oral administration of N-acetylcysteine (NACys) at a dose of 600 mg twice daily for eight weeks. The findings revealed that both MSCs and NACys led to significant reductions in creatinine, cystatin C, and reactive oxygen species levels compared to baseline measurements. However, the reductions in these biomarkers were significantly greater in patients who were treated with MSCs than those who received NACys. Additionally, MSC therapy resulted in greater enhancements in types 1 and 4 collagen levels when compared to NACys. The study highlighted that MSC treatment yielded significantly superior improvements

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in renal and systemic functional parameters compared to NACys after a four-week treatment period. The strict inclusion criteria of enrolling Chinese CRF patients with eGFR below 60 mL per minute per 1.73 m^2 ensured a homogeneous study population in terms of disease severity. Furthermore, the comprehensive and accurate collection of data on various efficacy parameters, including creatinine, cystatin C, TGF-β levels, reactive oxygen species, collagen levels, and renal/systemic functional parameters, allowed for a detailed evaluation of the effects of MSC therapy compared to NACys in CRF patients, providing valuable insights into potential treatment benefits and outcomes[25].

3.3. Application of MSCs in AKI

AKI is a complex condition characterized by dysregulated immune-mediated inflammation, which is pivotal in critical illnesses like burn injury, acute respiratory distress syndrome, acute liver failure, sepsis, and COVID-19[26]. MSCs have emerged as a promising therapeutic approach for modulating immune responses in inflammatory conditions. By secreting various molecules, MSCs can regulate immune cell responses and foster tissue repair. While MSCs have demonstrated efficacy in preclinical and early-phase clinical studies for conditions such as myocardial infarction and AKI, challenges persist in optimizing their delivery and persistence in the body. To address these challenges, a novel ex vivo MSC product, SBI-101, has been developed. SBI-101 immobilizes allogeneic bone marrow-derived MSCs in the extracapillary space of a hemofiltration device. This setup allows for controlled exposure of circulating blood cells to MSC-secreted factors. The study was a multicenter, randomized, double-blind, sham-controlled investigation into the safety, tolerability, and pharmacology of SBI-101 in adult subjects with AKI-dialysis undergoing continuous renal replacement therapy. Sixteen subjects participated in the trial, with 12 receiving active treatment (250×10^6 MSCs) and 4 receiving sham treatment.

Pharmacokinetic assessments revealed a dynamic secretion of proteins like IL-6, IL-8, MCP-3, and CXCL5 by MSCs with SBI-101 during the treatment course. A comparison of these factors in the extracapillary space between SBI-101 and sham treatment indicated enhanced activity in the active group. Limitations of the study included a small sample size and the lack of certain immune cell data for all patients. Future studies will focus on enrolling more patients, collecting additional immune profiling data, and exploring higher doses of SBI-101 to enhance efficacy and prolong pharmacodynamic effects. The development of innovative MSC-based therapies like SBI-101 holds promise for addressing dysregulated immune responses in critical illnesses such as AKI and CKD[27].

3.4. Application of MSCs in SLE

SLE is an autoimmune disease characterized by the presence of autoantibodies and multiorgan injury. MSCs have emerged as a potential treatment option for SLE due to their ability to differentiate into various cell types and their immunomodulatory effects on immune cells. A clinical trial investigated the use of UC-MSC infusion in the patients with SLE. Among 39 patients, 40 (97.5%) received two UC-MSC infusion at a one-week interval. One patient (2.5%) did not receive the second infusion due to uncontrolled disease progression. The study reported a high overall survival rate of 92.5% after 12 months, indicating a positive outcome for the majority of patients. Lupus disease activity, measured by the SLE Disease Activity Index score and British Isles Lupus Assessment Group score, significantly decreased after the UC-MSC infusion. Serum albumin levels improved, complement levels showed improvement, and anti-double-stranded DNA antibody levels decreased after MSC treatment. Renal function and proteinuria levels improved significantly after UC-MSC treatment. Hematopoietic and cutaneous system involvement also showed improvement[28]. El-Ansary et al. conducted a study involving three groups of subjects, and the results indicated that individuals in the SLE group displayed less anemia and showed greater advancements in renal function compared to the other groups throughout the follow-up period. Additionally, significant enhancement in kidney function tests was noted in this particular group, with elevated hemoglobin levels in comparison to the other groups[16].

4. FUTURE PERSPECTIVES

Despite the growing evidence of the therapeutic potential of MSC-based therapies in renal diseases, several challenges remain for their widespread clinical application. Most notably, there is a lack of standardized protocols regarding the source of MSCs, isolation and validation methods, dosage, and routes of cell administration, which has led to considerable heterogeneity across clinical studies. Furthermore, most of the current clinical trials are limited by small sample sizes, short follow-up periods, and variability in the outcome studied. These limitations make it difficult to draw definitive conclusions about the long-term efficacy and safety of MSC therapies.

Future research should focus on multicenter randomized clinical trials with standardized designs to better characterize the therapeutic efficacy of MSCs in CKD, AKI, and complications associated with kidney transplantation. Studies with long-term follow-up are

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Table 1. Summary of details from 18 clinical trials on MSC therapy for Renal Failure, including trial phase, MSC source and administration, patient demographics, clinical outcomes, and adverse events

Ref.	Author/ year	Phase/type of study	MSC source and type	Administration route	Dose and frequency	Patients	CKD type	Clinical outcomes	Follow-Up duration	Adverse events
[29]	Sabir 2026	Pilot interventional, double-blind randomized controlled trial	Allogeneic BM-MSCs	IV infusion	Single infusion of 30×10^6	78 adults	Diabetic nephropathy	Improved GFR and HbA1c	6 months	No significant adverse events reported
[30]	Carstens 2023	Not mentioned	Adipose-derived stromal vascular fraction	Bilateral renal artery catheterization	Single infusion (NR)	18 patients	Mesoamerican nephropathy (CKDu)	Safe, improved perfusion, and maintained renal function in some patients	36 months	No serious adverse events, treatment-related complications
[31]	Riordan 2022	Case report	Allogeneic UC-MSC	IV	Not specified	1 female, 42 years	Acute renal failure and IgA nephropathy	Improvement in kidney function	3months	Not mentioned
[19]	Zhang 2021	Pilot study	Autologous BM-MSC	Intra-arterial/ IV	5×10^6 (day 0) and 1×10^6 (7 days and 1 month later)	11 patients	Interstitial fibrosis and tubular atrophy post-kidney transplant	Kidney function improvement in 54.5%, 27.3% stable, 18.2% worsened. Decreased TGF-β1 and connective tissue growth factor expression	1 year	2 cases of infection and allergy
[25]	Shao 2021	Pilot study	Autologous BM-MSC	IV	$1–2 \times 10^6$ cells/kg	200 patients	CRF	Decreased Cr, Cys-C, TGF-β1, ROS Increased COL1, COL4	Not specified	Not specified
[27]	Swaminathan 2021	Phase I/II clinical NCT03015623	Allogeneic MSC	IV by NxStage System dialysis	300×10^6 cells (single dose)	15 Patients	AKI and systemic inflammation	Improvement in kidney function, decreased TNFα, IFNγ & Monocytes	18 months	None mentioned
[32]	Villanueva 2019	Pilot study	Autologous adipose Tissue MSC	IV	1×10^6 cells/kg	10 Patients	CKD	Stabilized eGFR; reduced proteinuria	12 months	Mild (transient fever)
[22]	Makhlough 2018	Safety Study	Autologous BM-MSC	IV	$1–2 \times 10^6$ cells/kg	7 patients	CKD	Safety of treatment confirmed, nonsignificant reduction in the rate of eGFR	18 months	Not mentioned
[21]	Rahyussalim 2017	Case report	Allogeneic umbilical cord MSC	Intrathecal and IV	16×10^6 (Three doses)	1 female, 62 ears	CRF and spinal cord entrapment	Improvement in kidney function and ability to move toes, creatinine reduced to 2 mg/dl	8 months	None mentioned
[33]	Kim 2017	Phase I	Autologous BM-MSC	IV	4×10^8 (Single dose)	1 male, 33 years	Renal insufficiency	Rapid deterioration of renal function after therapy	Short-term	Worsened Cr/clearance
[24]	Packham 2016	Phase 1/2	Allogeneic BM-MSCs (MPC, rexlemestrocel-L)	IV	$150\text{-}300 \times 10^6$ MPC	10 placeboes 20 diabetic nephropathies	Diabetic nephropathy (eGFR 20-50 ml/min/1.73m²)	stabilization or improvement in eGFR and mGFR GFR stabilization in the MSC group	12 weeks	No treatment-related serious adverse events
[28]	Wang 2014	Phase 2	Allogeneic UC-MSC	IV	Two infusions on days 0 and 7 (NR)	40 patients	SLE with lupus nephritis	Significant decrease in SLE Disease Activity Index and British Isles Lupus Assessment Group scores, reduced proteinuria, improved renal function	12 months	No transplantation-related adverse events

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[3]	EL-Ansary 2012	Pilot Study	Autologous BM-MSC	IV	$0.7–1.0\times10^6$ cells in 2 doses (1 week apart)	30 patients (22-68 years)	10 SLE-related GN, 10 kidney transplants, 10 controls	Significant improvement in creatinine and clearance in SLE group	6 months	None significant
[34]*	Stavas 2024	Phase 2	Renal autologous cells**	Bilateral percutaneous kidney injections	2 injections, 3 months apart (NR)	53 adults	Type 1 and type 2 diabetes-related CKD	Potential to preserve or improve kidney function, delay disease progression	Ongoing	No significant adverse events reported
[35]*	Stavas 2023	Phase 1	Renal autologous cells**	Percutaneous kidney cortex injections	2 injections, 7 ± 3 months apart (NR)	22 adults	Type 2 diabetes-related CKD	Improved eGFR slope, stable renal function in some patients	1 year	2 remote fatal adverse events unrelated to the treatment
[36]*	Stavas 2022	Not mentioned	Renal autologous cells**	Percutaneous subcortical kidney injections	2 doses, 7 ± 3 months apart (NR)	22 adults	Type 2 diabetes-related CKD	Improved eGFR slope, stabilized renal function	1 year	2 remote fatal adverse events unrelated to treatment
[37]*	Stavas 2021	Phase 1	Renal autologous cells**	Image-guided locoregional reinjection into renal cortex	2 doses at 6-month intervals (NR)	5 patients	Congenital anomalies of the kidney and urinary tract-associated CKD	No complications, potential to stabilize or improve renal function	Ongoing	No complications or adverse events
[38]	Humes 2003	Phase I/II	Human renal proximal tubule cells (RAD)	IV	Not specified	9 patients	Acute renal failure + Multiple Organ System Failure	Cardiovascular stability, metabolic activity	Not specified	Rapid and variable responses
[39]	Tumlin 2008	Phase II	Renal tubule cells (RAD)	IV	Single 24–72 h extracorporeal / 1 RAD cartridge	58 patients	ARF	Improved survival, faster kidney recovery	180 days	Expected profile for critically ill patients

*It appears that all these articles are derived from a larger overarching study; **Although renal autologous cells or rilparencel (REACT®) represents a regenerative autologous renal cell-based therapy, these cells do not strictly fulfill the established phenotypic and functional criteria of MSCs; NR: not reported

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useful for assessing sustained improvements in renal function, transplantation outcomes, and potential late adverse events after MSC administration.

Advances in cell manipulation, biomaterials, and novel MSC-based products such as SBI-101 may further enhance the efficacy and durability of MSC therapies. Also, an increasing emphasis on safety profiling and personalized medicine approaches could advance the optimization of MSC therapy according to individual patient characteristics and immunological status[40]. In addition, combination therapies that integrate MSCs with immunosuppressive agents or other regenerative strategies may be a promising approach to improve treatment outcomes in renal diseases, although MSC-based therapy as a regenerative and immunomodulatory strategy shows considerable promise. However, before routine clinical implementation can be achieved, it is crucial to address challenges related to transfer, monitoring, cost-effectiveness, and standardization of clinical protocols.

5. CLINICAL TRIALS

To investigate the future of cell therapy in the treatment of kidney diseases, we reviewed the website https://clinicaltrials.gov/ in May 2026. The analysis identified 52 studies; however, some of them were excluded from the review process due to different objectives, such as exosome-based therapies. Stem cell therapy trials for kidney disorders have been conducted globally, with notable studies in China, the US, Iran, and European countries (Fig. 4). The most commonly used cell types in these studies were MSCs derived from C-MSCs, adipose tissue (AD-MSCs), BM-MSCs, and Wharton's jelly, typically administered at doses of 1-5×

Fig. 4. (A) An analysis of clinical trials reveals that China (40%) and the United States (33%) lead in renal cell therapy trials. (B) Lupus nephritis (27%) and diabetic nephropathy (20%) are primary targets. (C) UC-MSCS and AD-MSCS account for a combined total of 47%; (D) IV delivery is used in 60% of trials, which remains the standard method.

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10^6 cells/kg via IV infusion. In specific cases targeting renal vasculature, intrarenal and intra-arterial delivery methods were also employed. The primary conditions addressed by these trials included diabetic nephropathy (38% of reviewed trials) and CKD (29%), followed by lupus nephritis (18%) and AKI (12%). Comorbid conditions such as type 1/2 diabetes, hypertension, and SLE were frequently reported alongside renal pathologies. Therapeutic mechanisms were focused on immunomodulation, particularly in autoimmune nephropathies as well as tissue regeneration through paracrine signaling. Safety assessments primarily focused on infusion-related reactions and tumorigenicity, while efficacy was evaluated based on improvements in eGFR (reported in 67% of trials), reduction in proteinuria (58%), and histopathological changes in biopsy-confirmed cases. Notably, second-generation trials have increasingly combined MSC therapy with conventional immunosuppressants, demonstrating synergistic effects in transplant rejection protocols. Despite promising results in phase I/II trials, heterogeneity in cell sources, dosing protocols, and outcome measures underscore the need for standardized phase III trials. Current evidence positions MSC therapy as a viable adjunct treatment for refractory nephropathies, particularly in cases where conventional therapies show limited efficacy. Further research should address long-term safety, optimal delivery routes, and biomarker-based patient stratification. Despite the limitations of existing studies, development of innovative MSC-based therapies holds promise for addressing dysregulated immune responses in critical illnesses such as AKI and CKD.

6. CONCLUSION

MSC-based therapies, as a promising regenerative and immunomodulatory approach, have recently received attention in the treatment of CKD, AKI, lupus nephritis, and complications associated with kidney transplantation. Most clinical studies have shown favorable safety profiles and suggested potential benefits, including improvements in kidney function, as well as reduction in inflammatory responses, fibrosis, and proteinuria. However, several factors contribute to uncertainty regarding the long-term efficacy and optimal treatment protocols for MSC therapy in kidney diseases. These factors include small sample sizes, heterogeneity in MSC sources and treatment protocols, varying outcome measures, and insufficient long-term follow-up data. Therefore, the effectiveness of MSC therapies remains unproven. To validate the therapeutic potential of MSCs and facilitate their transfer into routine clinical nephrology practice, large-scale multicenter randomized clinical trials with standardized methods are necessary in the future. In this review, several limitations should be acknowledged. First, the number of available clinical studies investigating MSC-based therapies for renal diseases remains limited, and many studies were conducted with relatively small sample sizes. Second, substantial heterogeneity existed among the included studies regarding the source of MSCs, dosing regimens, routes of administration, follow-up duration, and outcome measures, which limit direct comparison among studies. Third, several studies lacked long-term follow-up data, making it difficult to assess the durability and long-term safety of MSC therapy. In addition, this review included only English-language studies, which may have introduced language bias. These limitations highlight the need for larger, standardized, multicenter clinical trials in the future.

DECLARATIONS

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Generative AI and AI-assisted technologies

The authors used ChatGPT (OpenAI) for language editing and improving the clarity of the manuscript. All scientific content, interpretations, and conclusions were developed and verified by the authors.

Ethical approval

This project, focused on understanding Iranian Bioethics, has been registered under the code 22.IR.MUMS.MEDICAL.REC.1402.441.

Consent to participate

Not applicable.

Consent for publication

All authors reviewed the results and approved the final version of the manuscript.

Authors' contributions

SK: conceptualization, methodology, investigation, data curation, and writing—original draft; SGY: literature search, data analysis, and writing—review and editing; FF: investigation and data curation; OB: methodology, data analysis, and visualization; PE: supervision, validation, and writing—review and editing; ES: supervision, project administration, critical revision, and final approval of the manuscript. All authors read and approved the final manuscript.

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Data availability

Data sharing does not apply to this article, as no new data were created or analyzed in this study.

Competing interests

The authors declare that they have no competing interests.

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Supplementary information

The online version does not contain supplementary material.

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