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Unveiling hidden contaminants: a systematic quantification and characterization of microplastics in hemodialysis and peritoneal dialysis fluids

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Abstract

Microplastics (MPs) are an emerging environmental and biomedical concern due to their potential bioaccumulation and toxic effects. Given the extensive exposure of dialysis patients to large volumes of dialysate and water, the presence of MPs in dialysis solutions raises concerns regarding chronic exposure and systemic implications. This study systematically quantifies and characterizes MPs in hemodialysis (HD) and peritoneal dialysis (PD) fluids, investigating their sources and potential health risks. A total of 30 dialysis solution samples were analysed (revealing 36 suspect particles) using advanced spectroscopic techniques, including Fourier-transform infrared (FT-IR) spectroscopy, to identify polymer compositions. MPs predominantly fibers, were detected in all tested solutions, with polyethylene (PE), polyvinyl chloride (PVC), and ethylene-vinyl acetate (EVA) as the primary polymers. Statistical analyses confirmed significant variability in MP contamination across different dialysis fluids. Hemodialysis and peritoneal dialysis solutions show no statistically significant difference in MP concentration (HD: 0.29 ± 0.16 mp.L⁻¹, PD: 0.34 ± 0.02 mp.L⁻¹, $p = 0.86$). MP particles in HD solutions (1.31 ± 0.98 mm) are significantly larger than those in PD solutions (0.64 ± 0.43 mm) ($p = 0.030$). Despite similar MP concentrations, PD patients are estimated to be exposed to ~50% more MPs weekly than HD patients (9.57 ± 5.28 vs. 14.28 ± 0.84 mp. L⁻¹, $p < 0.001$). These findings highlight a potential, yet underrecognized, source of MP exposure in dialysis patients, necessitating further investigation into the implications of chronic MP absorption on renal function and systemic health. Regulatory policies should prioritize improved filtration techniques, alternative polymer-free materials, and stricter quality control measures to mitigate MP contamination in medical solutions. Future research should explore the long-term effects of MP exposure in dialysis-dependent individuals and refine analytical methodologies for contamination assessment.

Synopsis

This study reveals microplastic contamination in dialysis fluids, highlighting a previously unrecognized exposure route that may impact patient health and emphasizing the need for improved filtration, polymer-free materials, and stricter regulatory measures.

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Keywords Microplastics, Exposure, Dialysis, Human health

Introduction

Chronic kidney disease (CKD) is a progressive disorder characterized by sustained structural and functional impairments in the kidneys persisting for at least three months, ultimately impacting systemic homeostasis. The 2024 KDIGO Clinical Practice Guidelines define CKD as kidney damage or a glomerular filtration rate (GFR) below 60 mL/min/1.73 m² for at least three months, with implications for patient health [1]. The global burden of CKD remains significant, with an estimated 697.5 million individuals affected worldwide in 2017, reflecting a prevalence rate of 9.1% [2]. In advanced CKD stages, morbidity and mortality rise substantially, often necessitating renal replacement therapy (RRT) [3, 4]. The KDIGO 2024 guidelines emphasize individualized dialysis modality selection based on patient-specific factors, comorbidities, and lifestyle preferences.

Hemodialysis (HD) is a cornerstone therapy for end-stage CKD (G5), in which extracorporeal circulation allows blood filtration through a capillary dialyzer. This semipermeable membrane facilitates the removal of metabolic waste products while preserving electrolyte and fluid homeostasis. During HD, patients are exposed to 300–600 L of dialysate per week, composed primarily of water and essential solutes such as sodium, potassium, and calcium. In conventional hemodialysis, hydrostatic pressure gradients drive ultrafiltration (UF) to remove fluid from the patient's circulation (typically 1–3 L/session). Backfiltration of dialysate-derived contaminants may occur in high-flux HD but remains secondary to outward solute clearance. In contrast, hemodiafiltration—a hybrid technique combining diffusive/convective clearance—requires infusion of 20–45 L/session of online-generated substitution fluid directly into the bloodstream to counterbalance UF losses. This substitution fluid adheres to stricter ultrapurity standards than conventional dialysate [5, 6].

Peritoneal dialysis (PD) represents an alternative renal replacement modality that utilizes the peritoneal membrane as a natural semipermeable barrier, facilitating solute and fluid exchange between the peritoneal capillaries and the dialysate instilled into the abdominal cavity. PD solutions are prepackaged in sterile plastic containers, allowing for patient-administered home-based dialysis following structured training [7].

Microplastics (MPs) ranging in size from 1 nm to < 5 mm, have been detected in soil, water, and the atmosphere, raising concerns about their potential impact on human health through bioaccumulation in the food chain [8]. Evidence from animal studies indicates that MPs can accumulate in various organs and tissues, triggering

oxidative stress, inflammatory responses, and metabolic dysregulation [9, 10].

Microplastic-induced nephrotoxicity is a growing concern due to the widespread presence of microplastics in the environment and their potential to cause kidney damage. Studies have shown that exposure to polystyrene microplastics (PSMPs) can lead to oxidative stress, inflammation, and cellular damage in the kidneys of various animal models [11, 12]. These effects are primarily mediated through the generation of reactive oxygen species (ROS) and the activation of inflammatory pathways. Exposure to PSMPs results in altered kidney function markers, such as increased creatinine and urea levels, indicating impaired renal function. Histological changes, including glomerular tuft enlargement and fibrosis, have been reported, although the latter remains unchanged in some studies [13].

Growing concerns have emerged regarding the potential contamination of dialysis patients with MPs. These synthetic polymeric particles have been detected ubiquitously in environmental matrices, raising significant biomedical concerns due to their potential for systemic absorption, bioaccumulation, and toxicity. Recent pre-clinical studies indicate that MP exposure may trigger oxidative stress, inflammatory cascades, and metabolic dysregulation, exacerbating CKD-related complications [14]. The KDIGO 2024 CKD guidelines underscore the importance of monitoring environmental exposures, particularly in vulnerable patient populations, as dialysis filtration systems exhibit limited efficacy in removing MPs of specific dimensions [1]. Moreover, polymeric components of dialysis apparatus and PD solution storage containers may serve as endogenous sources of MP release, necessitating further investigation into their clinical implications. This study aims to systematically assess the extent of MP exposure among HD and PD patients during their treatment processes.

Materials and methods

Dialysate fluid handling and sampling procedure

In our center, conventional hemodialysis is performed without the use of online hemodiafiltration (HDF) systems. Thus, dialysate fluids are not prepared online but are supplied as pre-formulated acidic and basic concentrates. These solutions are delivered to the hospital in sealed 5- and 6-liter plastic containers and stored under standard conditions. During HD sessions, the acidic and basic components are automatically mixed with purified municipal water by dialysis machines to generate the final dialysate. All HD patients in this study received conventional HD three times per week, with each session

lasting approximately 4 h. For microplastic (MP) analysis, fluid samples were collected directly from the original, unopened containers of acidic and basic concentrates, before any contact with the dialysis machine or water treatment system. This allowed assessment of microplastic contamination originating solely from the dialysate solutions themselves.

In patients undergoing continuous ambulatory peritoneal dialysis (CAPD), dialysate was provided as commercially prepared solutions in sterile, 2-liter plastic-containing bags. All CAPD patients performed 3 manual exchanges per day as part of their routine dialysis regimen. For MP analysis, fluid samples were drawn directly from the unopened PD solution bags to evaluate potential microplastic contamination originating from the packaging or production process.

Physical characterization

This study systematically investigated the presence and characteristics of MPs in four solutions utilized in HD and PD. Prior to analytical procedures, each sample was homogenized by thorough shaking to ensure uniform distribution of microplastics. Filtration was performed using 47 mm diameter GF/F glass fiber filters (0.7 μm pore size) within a controlled laminar flow chamber. Post-filtration, filters were placed in Petri dishes and maintained under controlled temperature conditions to prevent external contamination.

The enumeration of MPs was conducted via stereomicroscopy, with meticulous documentation of physical attributes, including morphology and coloration. Photographic records were systematically captured to support visual analysis. Particle dimensions were measured using Leica LAS Image software, recording the longest dimension of fragmented particles and the full lengths of fibers. Furthermore, all particles underwent Fourier-transform infrared (FT-IR) spectroscopy for precise chemical characterization, ensuring a comprehensive evaluation of polymer composition.

Chemical characterization of microplastics

To rigorously determine the polymeric composition of microplastic particles, Fourier-transform infrared spectroscopy (FT-IR) was employed as a high-resolution analytical technique. A SHIMADZU IR Tracer-100 spectrophotometer was utilized for spectral acquisition, covering a broad wavelength range of 600–4000 cm^{-1} with a resolution of 4 cm^{-1} across 32 consecutive scans per sample, ensuring precise molecular characterization and reproducibility.

The acquired spectra were systematically analysed against an extensively curated reference database embedded within the instrument's analytical software. Polymer classification was established based on a spectral

concordance threshold of >70%, guaranteeing a robust and reliable identification framework. To further refine polymer differentiation, spectral overlays with reference spectra were performed, providing enhanced confidence in distinguishing synthetic from naturally derived polymeric structures. This rigorous analytical approach ensured a comprehensive, reproducible methodology for the precise classification of microplastic composition.

Quality assurance and quality control (QA/QC)

To minimize contamination and maintain analytical rigor, stringent quality control measures were implemented throughout the study. Laboratory personnel adhered to contamination control protocols, including the use of cotton laboratory coats and nitrile gloves during all experimental procedures. All analyses were conducted in a controlled laminar flow chamber to prevent airborne particulate contamination. All liquids used during the analysis were pre-filtered through membrane filters (0.2 μm pore size) to prevent microplastic contamination. Microscope-based observations were carried out in designated clean environments. Petri dishes containing moistened polycarbonate track-etched (PCTE) filters were systematically placed within the workspace to act as contamination traps. Any potential contamination was meticulously documented, and compromised particles were excluded from the final dataset to preserve data integrity. These rigorous QA/QC measures ensured that the findings remained scientifically robust, reproducible, and of high methodological precision.

Estimation of weekly microplastic exposure via dialysis fluids

To estimate weekly microplastic (MP) exposure from dialysis fluids, standard treatment protocols for hemodialysis (HD) and peritoneal dialysis (PD) were considered. For patients undergoing conventional HD, each session involved exposure to approximately 11 L of dialysate, delivered in two separate containers (5 L and 6 L). As all patients received HD three times per week, the total weekly dialysate exposure was calculated as 33 L per patient. Using the mean MP concentration detected in HD dialysate fluids (mean MP concentration in HD), weekly MP exposure was estimated using the formula:

Weekly MP exposure (HD) = 33 L \times mean MP concentration in HD ($\text{mp}\cdot\text{L}^{-1}$).

In patients receiving continuous ambulatory peritoneal dialysis (CAPD), the standard protocol included three exchanges per day with 2 L of dialysate per exchange, totaling 6 L daily and 42 L weekly. Weekly MP exposure for PD patients was calculated based on the mean MP concentration in PD dialysate fluids (mean MP concentration in PD):

Table 1 Microplastic contamination in dialysis solutions: packaging/lid material, sample volume, and physical characteristics

Sample	Volume (ml)	No. of samples analyzed	Packaging material	Total MP	Mean MP (mp. L ⁻¹)	Length (mm) ± SD
Hemodialysis (HD)						
1	5000	8	PE	7	0.18	1.05 ± 0.35
2	6000	8	PE	19	0.40	1.40 ± 1.11
Mean ± SD	-	-	-	-	0.29 ± 0.16*	1.31 ± 0.98**
Weekly MP exposure for one HD patient					9.57 ± 5.28***	
Peritoneal Dialysis (PD)						
3	2000	7	PVC	5	0.36	0.60 ± 0.40
4	2200	7	PVC	5	0.32	0.69 ± 0.50
Mean ± SD	-	-	-	-	0.34 ± 0.02*	0.64 ± 0.43**
Weekly MP exposure for one PD patient					14.28 ± 0.84***	
Total	-	30	-	36	0.31 ± 0.04	1.19 ± 0.91

MP: Microplastic, PE: Polyethylene, PVC: Polyvinyl chloride (* $p=0.86$, ** $p=0.030$, *** $p<0.001$)

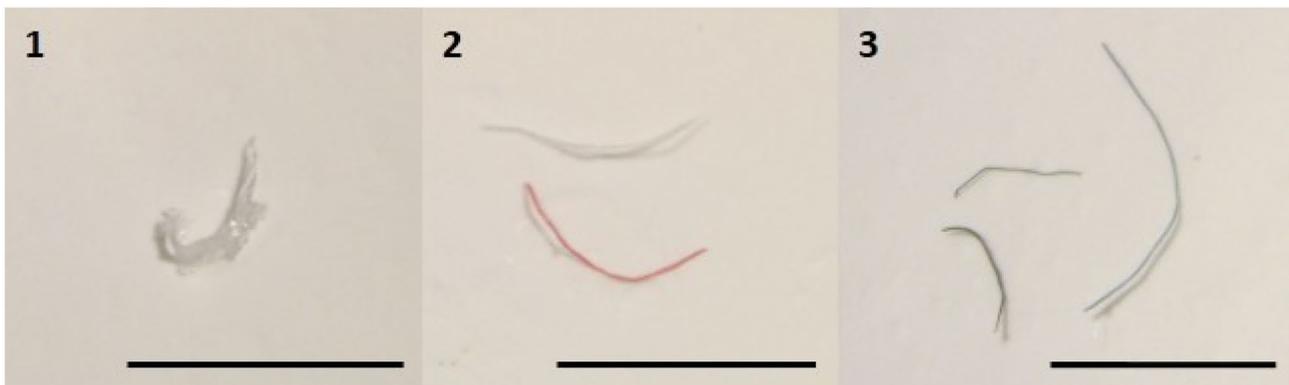


Fig. 1 Examples of microplastics identified in dialysis solutions (1: Polyethylene transparent fragment, 2: Cellulose red fiber and polyethylene terephthalate transparent fiber, 3: polyvinylchloride blue fibers, Scale: 1 mm)

Weekly MP exposure (PD) = 42 L × mean MP concentration in PD (mp·L⁻¹).

These calculations provided a basis for comparing the potential microplastic burden between HD and PD modalities.

Data analysis

Statistical analysis was conducted to evaluate the distribution and characteristics of microplastics in dialysis solutions. Descriptive statistics, including mean, standard deviation (SD) was calculated for total microplastic count, mean microplastic concentration (mp·L⁻¹), and particle size. The mean weekly MP exposure through dialysis fluids for HD and PD patient was calculated. Student's t-test was used for parametric variables and Mann-Whitney U-test was used for nonparametric variables. Yates correction Chi-square test and Fisher's exact test were used for comparison of qualitative data. All statistical analyses were conducted using SPSS (IBM SPSS Statistics v.26). A significance threshold of $p<0.05$ was used to determine statistical significance.

Results

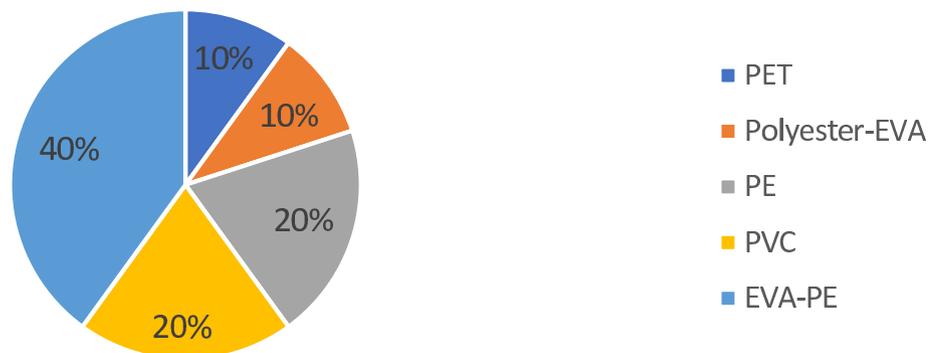
A total of 30 dialysis solution samples were analyzed, revealing 36 suspect particles. The detailed attributes of the analyzed samples are presented in Table 1. Among these, 35 were identified as fibers, while one was classified as a fragment (Fig. 1). The fragment measured 0.57 mm, whereas the fibers ranged in length from 0.11 to 4.41 mm (mean ± SD: 1.14 ± 0.91 mm). Overall, the detected microplastics in HD solutions varied in size from 0.15 to 4.41 mm (mean ± SD: 1.31 ± 0.98 mm), while those in PD solutions ranged between 0.11 and 1.32 mm (mean ± SD: 0.64 ± 0.43 mm). HD and PD solutions show no statistically significant difference in MP concentration (HD: 0.29 ± 0.16 mp·L⁻¹, PD: 0.34 ± 0.02 mp·L⁻¹, $p=0.86$). MP particles in HD solutions (1.31 ± 0.98 mm) are significantly larger than those in PD solutions (0.64 ± 0.43 mm) ($p=0.030$). Despite similar MP concentrations, PD patients are exposed to ~50% more MPs weekly than HD patients (9.57 ± 5.28 vs. 14.28 ± 0.84 mp·L⁻¹, $p<0.001$). In conclusion, while PD patients experience higher weekly MP exposure, HD solutions contain significantly larger MPs.

The concentration of microplastics in dialysis solutions ranged from 0.18 to 0.40 particles·L⁻¹. The highest

Table 2 Physical characteristics (shape and colour) of microplastics

Sample	Fiber				Fragment Transparent	Total (mp)
	Transparent	Blue	Red	Black		
1 (HD)	3	0	1	2	1	7
2 (HD)	2	6	0	11	0	19
3 (PD)	0	2	0	3	0	5
4 (PD)	0	1	0	4	0	5
Total	5	9	1	20	1	36

HD: Hemodialysis, PD: Peritoneal dialysis, MP: Microplastic

**Fig. 2** Composition of synthetic polymers (%) found in dialysis solution

microplastic concentration was recorded in Sample 3, whereas the lowest was found in Sample 1 (Table 2). Microplastics exhibited a range of colors, including transparent, blue, red, and black. Notably, Sample 1 was packaged in a bottle with a red cap, while Sample 2 had a blue cap, suggesting a possible contamination source from cap material. Conversely, Samples 3 and 4 were stored in transparent packaging, reinforcing the hypothesis that microplastic contamination may originate from manufacturing processes.

FTIR-based polymer identification and source attribution

FTIR spectroscopy revealed that 50% of the identified polymers in dialysis solutions were synthetic, while the remaining 50% were composed of natural cellulose-based materials. Among the synthetic polymers, ethylene vinyl acetate (EVA)-polyethylene (PE) accounted for the highest proportion (40%), followed by polyethylene (PE) (20%), polyvinyl chloride (PVC) (20%), polyethylene terephthalate (PET) (10%), and polyester-ethylene vinyl acetate (EVA) (10%) (Fig. 2). The diversity of polymer compositions underscores the multifaceted nature of dialysis fluid contamination, which stems not only from intrinsic material properties required for medical applications but also from external leaching sources, including packaging and industrial processing steps.

Discussion

The presence of microplastics (MPs) in dialysis fluids has emerged as a significant concern in nephrology due to their potential implications for patient safety. Given the high volumes of water utilized in hemodialysis (HD) and peritoneal dialysis (PD), patients undergoing these treatments may be at increased risk of MP and associated toxic chemicals exposure. Building on our findings, we analyse MP contamination in dialysis fluids, focusing on its physical and chemical properties, exposure routes, and nephrotoxic potential. Recent research highlights systemic risks, necessitating improved filtration, polymer-free materials, and stricter regulations to reduce MP exposure in dialysis patients.

Studies have detected MPs in human organs, including the kidneys, suggesting their potential for bioaccumulation and nephrotoxicity [11–14]. MP contamination in dialysis fluids can originate from multiple sources, including water supply, dialysis equipment, and packaging materials. The reliance on municipal water sources, which may already contain MPs, underscores the importance of efficient purification systems. Reverse osmosis (RO) and ultrafiltration are commonly employed to remove contaminants, yet recent findings indicate that these filtration methods may not be entirely effective in eliminating MPs, particularly smaller nanoparticles. Additionally, the materials used in dialysis systems—such

as polyethylene (PE), polyvinyl chloride (PVC), and polysulfone—have been identified as potential sources of MPs due to material degradation over time [15]. Packaging materials and plastic storage containers may also contribute to contamination, emphasizing the need for alternative biocompatible materials with reduced plastic content. Our study confirmed that the composition of the analyzed dialysis solution packaging materials predominantly consisted of polyethylene (PE) and polyvinyl chloride (PVC) (Table 1), establishing a direct correlation between the detected polymers in dialysis fluids and the packaging materials. These findings suggest that packaging-related polymer degradation and leaching may be one of several contributing sources of microplastic contamination in dialysis solutions necessitating further investigation into mitigation strategies and alternative material development. This aligns with existing literature demonstrating that polymer degradation, occurring through environmental stressors and mechanical handling, can introduce MP contaminants into pharmaceutical and medical solutions. Given the extensive handling, transportation, and storage conditions to which dialysis solutions are subjected, the potential for MP contamination is considerable. These findings underscore the necessity of stringent regulatory oversight and the development of alternative, biocompatible materials to minimize polymer migration and enhance dialysis fluid purity.

In addition to synthetic polymers, a notable proportion of particles identified in dialysis fluids consisted of natural cellulose-based materials, including cellulose and cellulose acetate. Although these materials are generally considered biodegradable and less persistent than synthetic polymers, their presence in sterile medical fluids is nonetheless concerning, as it suggests particulate intrusion at some point in the production or handling chain. Possible sources include cotton-based materials such as filters, gloves, or cleaning cloths used during manufacturing or packaging; cellulose-derived components of container linings; and airborne fibers from paper or textile products present in the production environment. Despite the implementation of strict contamination control protocols during laboratory analysis, the detection of these materials underscores the need for improved particle exclusion strategies during fluid production, storage, and administration processes.

Recent studies have confirmed the presence of MPs in human kidney tissues and urine, raising concerns about their potential bioaccumulation and long-term toxicological effects [16]. MPs have been detected in renal tissues with sizes ranging from 1 to 29 μm , and their chemical composition often includes polyethylene and polystyrene—common polymers found in dialysis materials. Prolonged exposure to MPs has been associated with increased levels of blood urea nitrogen and creatinine,

indicative of compromised renal function. These findings suggest that the kidney, as a primary organ for waste filtration, is a critical target for microplastic deposition. Smaller MPs (600 nm) tend to aggregate within kidney tissues, while larger particles (4 μm) remain in the extracellular matrix, suggesting a size-dependent bioaccumulation mechanism. While large microplastic particles (e.g., in the millimeter range) are unlikely to cross dialysis membranes due to size exclusion, their presence in fluids may indicate the potential for fragmentation into smaller particles. Nanoplastics and submicron-sized microplastics, which may escape conventional filtration, present a more plausible risk for translocation into the bloodstream. Further research is required to assess the permeability of dialysis membranes to particles in the lower micro- and nanoscale ranges and to evaluate patient exposure risks.

Microplastic exposure has been linked to several pathological mechanisms, including oxidative stress, inflammatory cytokine release, and immune dysregulation. Studies using *in vivo* and *in vitro* models have shown that MPs can trigger the upregulation of inflammatory mediators such as tumour necrosis factor- α (TNF- α), interleukin-6 (IL-6), and monocyte chemoattractant protein-1 (MCP-1), leading to renal inflammation and cellular damage [17]. Beyond inflammation, MPs have been implicated in altering cellular metabolism and promoting fibrosis. The persistent exposure to MPs in chronic kidney disease (CKD) patients may accelerate the progression of CKD by inducing fibrotic changes in renal tissues. The presence of MPs in dialysis fluids may exacerbate inflammation, oxidative stress, and fibrosis in renal tissue which results in loss of residual renal function. As environmental nephrotoxins gain recognition, further research is needed to assess MPs' role in CKD progression and fibrosis [18].

Chronic inflammation is prevalent in dialysis patients due to various factors, including the presence of dialysis catheters, recurrent infections, and ongoing immune activation. This persistent inflammatory milieu has been implicated in the pathogenesis of erythropoiesis-stimulating agent (ESA) resistance, contributing to refractory anemia, increased morbidity, and heightened mortality risk. While established causes of systemic inflammation in this population are well recognized, a subset of dialysis patients presents with unresolved inflammatory activation, where conventional etiological investigations yield inconclusive findings. Given the emerging evidence linking MP exposure to systemic inflammation, it is imperative to consider MPs as a potential, albeit under-recognized, contributor to the inflammatory burden in dialysis patients [19]. Addressing this concern necessitates a proactive approach, including stringent dialysis water purification protocols and the development of

polymer-free biocompatible dialysis materials. Given the potential implications of MP-induced inflammation, further investigation into its mechanistic pathways and impact on long-term renal outcomes is warranted. A deeper understanding of the interaction between MPs and nephropathic processes may inform targeted interventions aimed at mitigating inflammation and improving clinical outcomes in dialysis-dependent patients.

Further research should explore alternative dialysis system materials that minimize MP release, as well as advancements in water purification technology to improve patient safety. Investigations into the efficacy of existing filtration systems and the development of novel polymer-free membranes could provide meaningful solutions. Additionally, efforts should be made to assess the cumulative impact of MP exposure in dialysis patients, with particular focus on renal fibrosis, oxidative stress, and immune responses. Regulatory bodies must strengthen quality control standards for dialysis fluids and equipment to mitigate MP contamination risks. Incorporating stricter manufacturing guidelines and periodic assessment of dialysis system components for potential MP leaching is crucial. Furthermore, interdisciplinary collaborations between nephrologists, material scientists, and environmental researchers could facilitate the creation of safer dialysis environments. By integrating these measures, the long-term health implications of MPs in dialysis patients can be better understood and mitigated.

In a recent study, the potential number of MPs that can penetrate the kidneys of patients during dialysis treatment was estimated as 0.0021–3768 mp/week, considering water consumption values of 300–600 L/week for patients having 1 or 2 HD treatments per week, respectively [15]. In the present study, the occurrence and characterization of MPs in HD and PD fluids were assessed for the first time. The potential number of MPs that can penetrate the kidneys of dialysis patients during treatment through HD and PD fluids was estimated as 9.57–14.28 mp/week. This is considerably lower compared to results of the evaluation study that considered the total water uses during dialysis treatment.

In this study, other units that could potentially cause MP contamination during dialysis have not been examined. Future studies should investigate all equipment, devices, and fluids that could contribute to contamination during dialysis including the MP removal efficiency of membrane filters. Additionally, considering that dialysis units are used over many years, the leaching of MP associated toxic chemicals to which patients are exposed during treatment should be investigated.

Conclusion

The extensive use of plastic in HD and PD systems, including dialyzer membranes, tubing, and storage containers, poses a risk of microplastic contamination. This study confirms microplastic presence in dialysis solutions, raising concerns about chronic patient exposure and potential health risks. The findings presented here are based on pre-packaged dialysis fluids and may not fully represent the particle profile of online-prepared fluids used in routine hemodialysis, which can vary depending on water treatment systems, infrastructure, and clinical protocols.

These findings have critical implications for nephrology and regulatory policies, emphasizing the need for further research into plastic-derived toxicants in dialysis materials. Understanding these interactions can lead to safer polymer alternatives and improved manufacturing standards.

Future studies should assess the long-term impact of microplastic exposure on renal function, systemic toxicity, and patient survival. Advancements in polymer analysis will be essential to enhance contamination detection, ensuring dialysis fluid safety and better clinical outcomes.

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Author contributions

E.K, K.K and U.A conceptualized and designed the study. K.K and Y.S.K collected and analyzed the data. E.K performed and interpreted the statistical analyses. K.K and Y.S.K drafted the initial manuscript. E.K and U.A critically reviewed and revised the manuscript. All authors reviewed and approved the final version of the manuscript.

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Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable. This study did not involve human participants or animal subjects.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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