*Desalination and Water Treatment*
www.deswater.com

doi: 10.5004/dwt.2023.29232

284 (2023) 72–80
February

# Monitoring the microbiological quality of dialysis water: a case study in selected hemodialysis units in Amman, Jordan before and during COVID-19 pandemic

Nivin Al Alami[a,*], Nourhan H. AbdelAllah[b,c], Yasser Gaber[b,d], Khaldoun Shatanawi[e]

[a]*Water, Energy and Environment Center, The University of Jordan, Amman 11942, Jordan, email: n.alami@ju.edu.jo*
[b]*Department of Microbiology and Immunology, Faculty of Pharmacy, Beni-Suef University, 62511 Beni-Suef, Egypt, emails: nourhan.hassan@pharm.bsu.edu.eg (N.H. AbdelAllah), yasser.gaber@pharm.bsu.edu.eg (Y. Gaber)*
[c]*Viral lab, Central Administrative of Biological, Innovative Products and Clinical Trials, Egyptian Drug Authority, Giza 12654, Egypt*
[d]*Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmacy, Mutah University, Al-Karak 61710, Jordan*
[e]*Civil Engineering Department, School of Engineering, The University of Jordan, Amman 11942, Jordan, email: kshatanawi@ju.edu.jo*

Received 27 August 2022; Accepted 19 December 2022

**ABSTRACT**

Water treatment systems play an essential role in dialysis therapy. The control of bacteriological water quality is vital to ensure a better quality of hemodialysis patient's life. The current study assessed the microbiological quality of the hemodialysis water system of four hemodialysis centers located in major public health centers in Amman, Jordan (Hemodialysis centers A, B, C, and D). Their water samples were collected monthly from the dialysis machine's water inlet before and during the COVID-19 pandemic between 2018 and 2021. Total heterotrophic bacterial counts (TC), detection of *Pseudomonas aeruginosa*, and bacterial endotoxin (BE) concentrations were examined. According to international guidelines, most of the TC and BE results were within acceptable levels. However, some points were outside the limits, in addition to *Pseudomonas aeruginosa* being detected as well. These data indicated that the centers studied should revise the quality control management of their hemodialysis. This research emphasizes the importance of regular monitoring, maintenance, and development of effective water treatment systems to avoid bacterial growth and the production of biofilms, even in pandemic situations.

*Keywords:* Microbial quality; Water; Hemodialysis; Endotoxins; Contamination

## 1. Introduction

Patients undergoing hemodialysis are subjected to a dialysis fluid, approximately 120–150 L, per dialysis session. Hemodialysis sessions are usually held three times a week for approximately 3–4 h per session to ensure patients' health. Effective monitoring of the hemodialysis quality is unquestionably linked to higher survival rates and fewer hospitalizations among dialysis patients [1]. This monitoring aims to ensure that the dialysis water system meets the specific guideline targets and detects any unforeseen risks. Therefore, it is crucial to regularly assess the hemodialysis system, particularly the dialysis water, to improve the clinical impact of hemodialysis sessions.

The quality of dialysis water and the dialysate fluid is mainly depending on the quality of the water source, the public water supply, and the design of the water treatment units [2]. The public water supply is usually the main source of the hemodialysis system. Public drinking water is treated, purified, and then transported through a distribution system within a hemodialysis center, where it is used to prepare dialysate concentrates. All of these treatment steps provide an opportunity for microbial growth (oligotrophs) if the water is contaminated and not adequately

* Corresponding author.

monitored [2]. The water quality from the filtration system used for dialysis is critical to prevent chemical and bacteriological contaminations of the dialysate in the patient's bloodstream [3,4]. The Association for the Advancement of Medical Instrumentation (AAMI) put thresholds for filtered water to be accepted for hemodialysis purposes. The maximum allowed level of the viable bacterial count was set to be 200 CFU/mL. In comparison, the threshold for endotoxin concentrations was set to be <2 EU/mL, in the case of the European Pharmacopoeia, the levels are set as follows 100 CFU/mL and <0.25 EU/mL, respectively [2,5–7].

Contamination of the dialysis water with specific microorganisms creates catastrophic problems for the patients. Among these problems is contamination with *Pseudomonas aeruginosa*, an opportunistic pathogen with a high potential for untreatable infection. *P. aeruginosa* is a Gram-negative bacterium, and it has served as a surrogate indicator for the presence of other opportunistic pathogens [8]. It is considered one of the most common contaminants in dialysis water systems due to the ability to form biofilms in the piping systems and consequently act as a focus for shedding bacteria and endotoxins into the water supply [9].

Bacterial contamination in hemodialysis water can have serious complications ranging from pyrogenic reactions, including chills, fever, myalgia, nausea, and headaches to septicemia [10,11]. To minimize microbial risk, a preventive measure strategy must be applied to control bacteria and biofilms in hemodialysis units, including the use of chemicals such as peracetic acid with hydrogen peroxide, or physical disinfection methods such as ultraviolet radiation and ozone [3].

On 26 January 2020, at the beginning of the COVID pandemic, the National Epidemics Committee and Health Ministry (NECHM) in Jordan dedicated specific hospitals to treat infections and prepared multiple measures to handle the arrival of coronavirus in the country. Five weeks later, the country's first case on discovered on March 2 [12].

Several studies discussed the impact of the COVID pandemic on the healthcare system, especially centers dealing with vulnerable patients such as dialysis patients [13–17]. This impact emphasized the need to maintain and disinfect the hemodialysis water treatment system. However, they did not emphasize the importance of restricted testing and monitoring of dialysate water. Therefore, these measurements should reduce the chance of further complications for dialysis patients and reduce the burden on healthcare facilities during the pandemic.

The major objective of the current study was to monitor the level of bacterial contamination and their endotoxin concentration in four hemodialysis units located in major public health centers in Amman, Jordan, before and during the COVID pandemic from 2018 to 2021. Additionally, we discuss the possible reasons that may lead to the unacceptable microbial quality of used water.

## 2. Materials and methods

### 2.1. Sampling locations and time interval

The study was carried out to include four hemodialysis centers in Amman, Jordan. The hemodialysis centers were identified as units A, B, C, and D. Samples were collected each month, including the period of the COVID-19 pandemic from January 2018 to January 2022. Details of the hemodialysis centers are represented in Table 1.

### 2.2. Characteristics of water treatment systems and water disinfection

The community water supply is the main source of the dialysis water system in these hemodialysis centers. Most dialysis units are equipped with water treatment systems that use several devices and processes for optimum water purification. The water treatment systems are usually composed of multistep treatment processes and are summarized as follows: sand filter, particulate 5 μm filter, an activated carbon filter to remove chlorine additives from the source water, particulate 5 μm microfilter, a softener, and reverse osmosis (RO) membranes. The role of the RO membrane is to remove up to 95%–99% of dissolved inorganic elements, such as ions of metals and salts, chemicals, and organic compounds, as well as bacteria, endotoxins, and viruses. Filtered water is treated with UV radiation (260 nm) using germicidal ultraviolet lamps and then kept in a storage tank. The treated water is then passed through 0.2 μm filters; these systems can remove both bacteria and endotoxins. The filtered water is distributed by a hydraulic circuit without dead space to the dialysis machines. The schematic representation of a typical water treatment system for centers A, B, C, and D is illustrated in Fig. 1. The water is continuously

Table 1
Hemodialysis centers in Amman, Jordan

| Hemodialysis centers | Center A | Center B | Center C | Center D |
|---|---|---|---|---|
| Age of hemodialysis center (y) | 3 | 5 | 5 | 3 |
| Average number of dialysis sessions (month) | 1,098 | 39 | 25 | 85 |
| Number of hemodialysis machines | 28 | 2 | 5 | 6 |
| Total number of machines in operation (2018–2021) | 23 | 2 | 3 | 3 |
| Average capacity of treated water storage ($m^3$) | 4 $m^3$ in stainless steel tank | 1 $m^3$ in a food-grade polyethylene material tank | 2 $m^3$ in a food-grade polyethylene material tank | 2 $m^3$ in stainless steel tank |

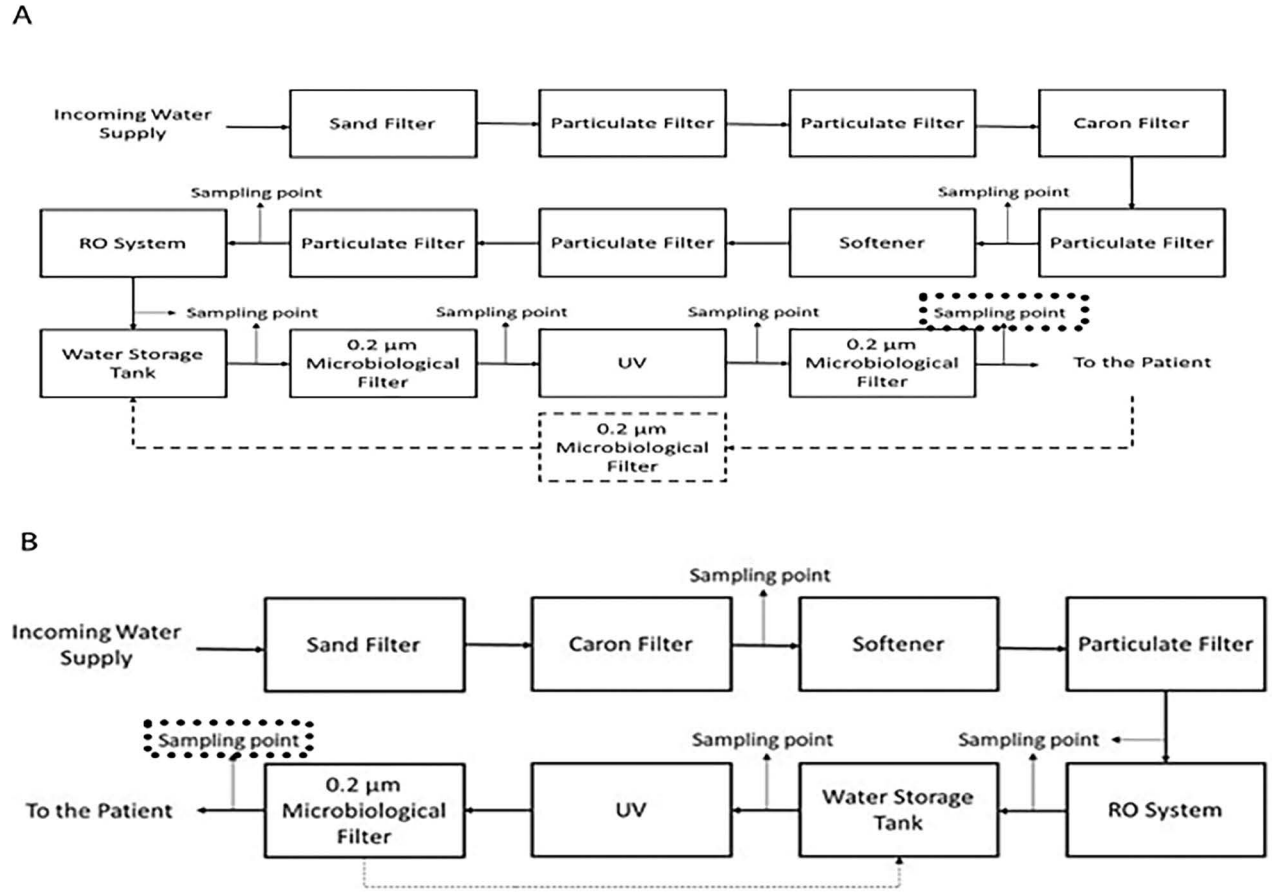


Fig. 1. Diagram explaining the water treatment system of Hemodialysis units where figure A represents Center A and C. While, figure B represents Center B and D.

circulated in the distribution loop for both water treatment systems. Carbon filters are replaced regularly every year. Besides, routine disinfection of the water systems is carried out every 40 d by (hydrogen peroxide/peracetic acid) with a volume ratio of 1:1. Shock disinfection was only applied in response to the increase in endotoxin concentration above 2 EU/mL and/or presence of *P. aeruginosa* in the water system. The shock treatment program consists of treatment with sodium hydroxide (NaOH), hydrogen peroxide with peracetic acid, and ozone disinfection.

### 2.3. Water sampling

Water samples were collected from the main water line that came from the water treatment system directly to the dialysis unit and from the connection of the dialysis machine near the patient's bed. Water samples were collected in 250 mL sterilized Pyrex® bottles containing 0.3 mL of 3% solution sodium thiosulfate ($Na_2S_2O_3$) as a neutralizing agent [18]. Each sample was collected aseptically after 3–5 min of a free water flush. For bacterial Endotoxin sampling, water samples were collected in a 25 mL non-pyrogenic tube. Using an icebox, the water samples were transported within 2 h to the Laboratory of Water Microbiology, at the Center for Water, Energy, and Environment of the University of Jordan.

### 2.4. Total heterotrophic bacterial count and detection of *Pseudomonas aeruginosa*

To recover surviving bacteria, the water samples were examined by membrane filtration as a concentration method, according to the Standard Methods for Examination of Water and Wastewater protocols [18]. To quantify the total heterotrophic bacterial counts under aseptic conditions, 100 mL of water sample was filtered on 0.45 µm pore size, 47 mm diameter (Sartorius®). The membrane filter was immediately removed with sterile forceps and cultured either on (R2A) a solid nonselective culture media agar (Thermo Scientific™ Oxoid™) or R2A agar plates were incubated at 35°C ± 0.5°C for 48 h. M-PA-C agar was used to detect *P. aeruginosa*; plates were incubated at (41.5°C ± 0.5°C) for 72 h (colonies were assessed morphologically by Gram stain, catalase test, oxidase test, and casein hydrolysis). The number of heterotrophic bacteria were expressed as colony forming units per milliliter (CFU/mL) [18]. As a positive control, the *P. aeruginosa* ATCC10145 strain (Microbiologics®, Inc., St. Cloud, MN) was activated and cultured [8,18].

### 2.5. Chromogenic test for bacterial endotoxins (BE)

The LAL assay method was used to detect endotoxin in water samples (reference?). Endosafe®-PTS™. Single-use

cartridges were purchased from Charles River Laboratories and used according to the manufacturer's instructions to measure endotoxins in water samples (EU/mL). The Endosafe®-PTS™ provides quantitative endotoxin results in approximately 15 min, with an assay sensitivity of 5.0–0.05 EU/mL. A positive control using a standard endotoxin solution was performed in conjunction with the test experiment. The incubation temperature was set at 37°C ± 1°C as recommended by the manufacturer.

## 3. Results and discussion

In the current study, four public dialysis centers were monitored for 4 y (2018–2022), during which water samples were collected for bacteriological analysis before and during the COVID pandemic. For center A, no detectable heterogenous bacteria or *P. aeruginosa* were detected in the samples collected before and during the COVID pandemic. This may explain the insignificant detectable concentrations of endotoxins in the examined water samples, in which the average concentrations were (0.06 and 0.08 EU/mL) before and within the pandemic, respectively.

The results obtained from center B showed that total bacterial counts were lower in the 2 y before the pandemic than in the next 2 y as shown in Fig. 2A. The highest TC was found in 2021. However, the TC of all samples was within the acceptable range (<200 CFU/mL) except for one sample which was collected in May 2018 (>200 CFU/mL)), as shown in Fig. 2A. On the contrary, the mean bacterial endotoxin during the pandemic was higher than in the previous 2 y, as shown in Fig. 2B. Regarding endotoxins, it was found that approximately 25% of samples had endotoxin levels beyond the acceptable limit (>2 EU/mL) during 2018 as shown in Fig. 4A. Furthermore, the growth of *P. aeruginosa* was consistently detected in the water samples collected in 2018 from March to July.

The total bacterial count for all collected samples of center C was <200 CFU/mL) during the study period, and the mean of the results before and during the pandemic was comparable as shown in Fig. 2C. The growth of *P. aeruginosa* was found in one sample in April 2018 as shown in Fig. 3B. However, there was a downtrend in endotoxin concentrations which notably decreased from 2018 to 2021 as presented in Fig. 2D. Hence, the mean results of BE in center C before the pandemic were remarkably higher than the results during the pandemic.

Although the TC mean results of center D from 2018 to 2019 (before the pandemic) were lower in comparison to the following 2 y (2021–2022), one sample in December 2018 showed that the TC was >200 CFU/mL by at least of two folds as shown in Fig. 2E. In addition, the growth of *P. aeruginosa* was detected in 50% of water samples collected before the pandemic mostly in 2018 as in Fig. 3C. However, the endotoxin content in the water samples was within the limit of the guideline value of the AAMI (<2 EU/mL) (Fig. 4C). It was found that the mean bacterial endotoxin during the pandemic was lower than in the previous 2 y (Fig. 2F) and there was no growth of *P. aeruginosa* in all water samples tested.

Hemodialysis is an important treatment for people with renal failure, improving their quality of life and, for some, being their only hope of survival. The microbial quality of water used in hemodialysis centers is the main concern, as contamination can lead to severe patient complications. During the COVID-19 pandemic, all health systems worldwide were exposed to tremendous pressure, this pressure emphasized the importance of good healthcare care management and monitoring systems to reduce hospitalization time and mortality risk. The current research aimed to evaluate the water treatment systems supplying hemodialysis units with treated water in four selected healthcare settings in Jordan before and during the COVID pandemic. Water samples were selected in which the water composition was uniform, under the most unfavorable conditions (e.g., the highest possible contamination points such as unprotected sources and low-pressure zones), and at points that mainly served the highest number of patients.

In general, our findings showed that the water quality could be affected by the design of the hemodialysis unit; the microbial quality of water examined at centers A and C shared the same design and was found to be better than the other two centers. All TC results of these two centers were within the AAMI acceptable threshold (<200 CFU/mL) during the duration of the study. The recently renovated center (center A) showed no detected bacteria over the 4 y. However, the mean of the TC of center C was the lowest among the three two centers. Furthermore, approximately 96% of samples collected from center C had TC lower than 100 CFU/mL), including the only incidence of growth of *P. aeruginosa* during April 2018. This was also confirmed by the results of the examined bacterial endotoxin content (less than 0.5 EU/mL) which is significantly lower than those of the other two centers. These findings could be explained by the presence of the additional particulate filter before the central reverse osmosis (RO) and another microbiological membrane filter (0.2 μm) after the storage tank in hemodialysis units located at centers A and C. It is clear from the microbiological analysis that the installation of two pyrogenic microbiological membrane filters gave excellent results compared to those of centers B and D. This implies the importance of adding a second pyrogenic membrane filter unit after the water storage tanks. The design of the water piping system should be highly considered, particularly connection fittings and joint points between the distribution loop and the dialysis machine. The pipe connection fittings prevent cross-connections between the machine supply and machine drain which help to avoid cross-contamination. The tubing should also avoid incorporating joints, dead-end pipes, and old branches and taps that can harbor bacteria and lead to the formation of biofilm. Our findings are consistent with an Italian study that reported that the increasingly extensive use of monitors and an ultrafilter for cold dialysate filtration led to good water microbial quality [19].

Surface waters typically contain endotoxin from Gram-negative bacteria and some types of blue-green algae. However, the chlorinated water supplies usually contain low levels of endotoxins and little water microflora; accordingly, endotoxins were detected in center A hemodialysis, despite the absence of heterotrophic bacteria. For that reason, the storage tank should be routinely drained and disinfected with an EPA-registered product.

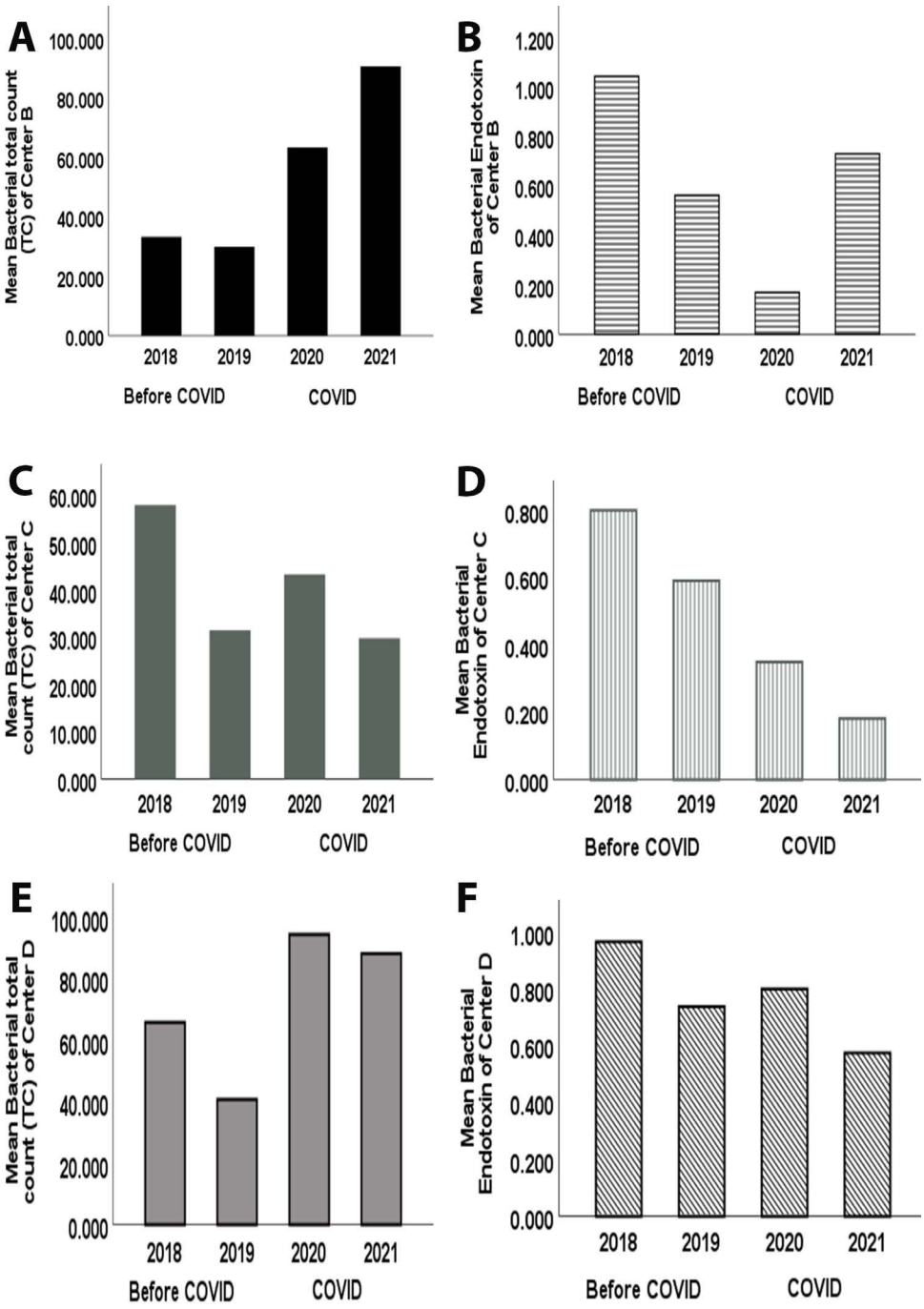


Fig. 2. Bar chart represents the mean results for the bacterial total count and bacterial endotoxin of Hemodialysis centers

The occasional growth of *P. aeruginosa* in RO membranes and/or in the tubing is a very serious issue. *P. aeruginosa* is an opportunistic pathogen, it proliferates rapidly in dialysis water systems and possesses a harmful effect on immunocompromised patients, and may cause infections such as septicemia and toxemia in dialysis patients through the production of toxin A [6,20]. Many articles show that *P. aeruginosa* can colonize water distribution systems and RO membrane filters and may form microbial biofilms, it produces slime that causes adhesion to the water system and increases its resistance to different biocides [21]. *P. aeruginosa* can change from a planktonic form to a sessile form that with its exo-polysaccharide production help colonizing other microorganisms [22]. This biofilm formation continues to cause recurrent contamination that affects the efficiency of RO membranes and it is difficult to remove with regular disinfection procedures [23,24]. The overall microbiological quality of water intended for hemodialysis purposes depends on several steps of filtration and disinfection techniques and the proper quality control practices

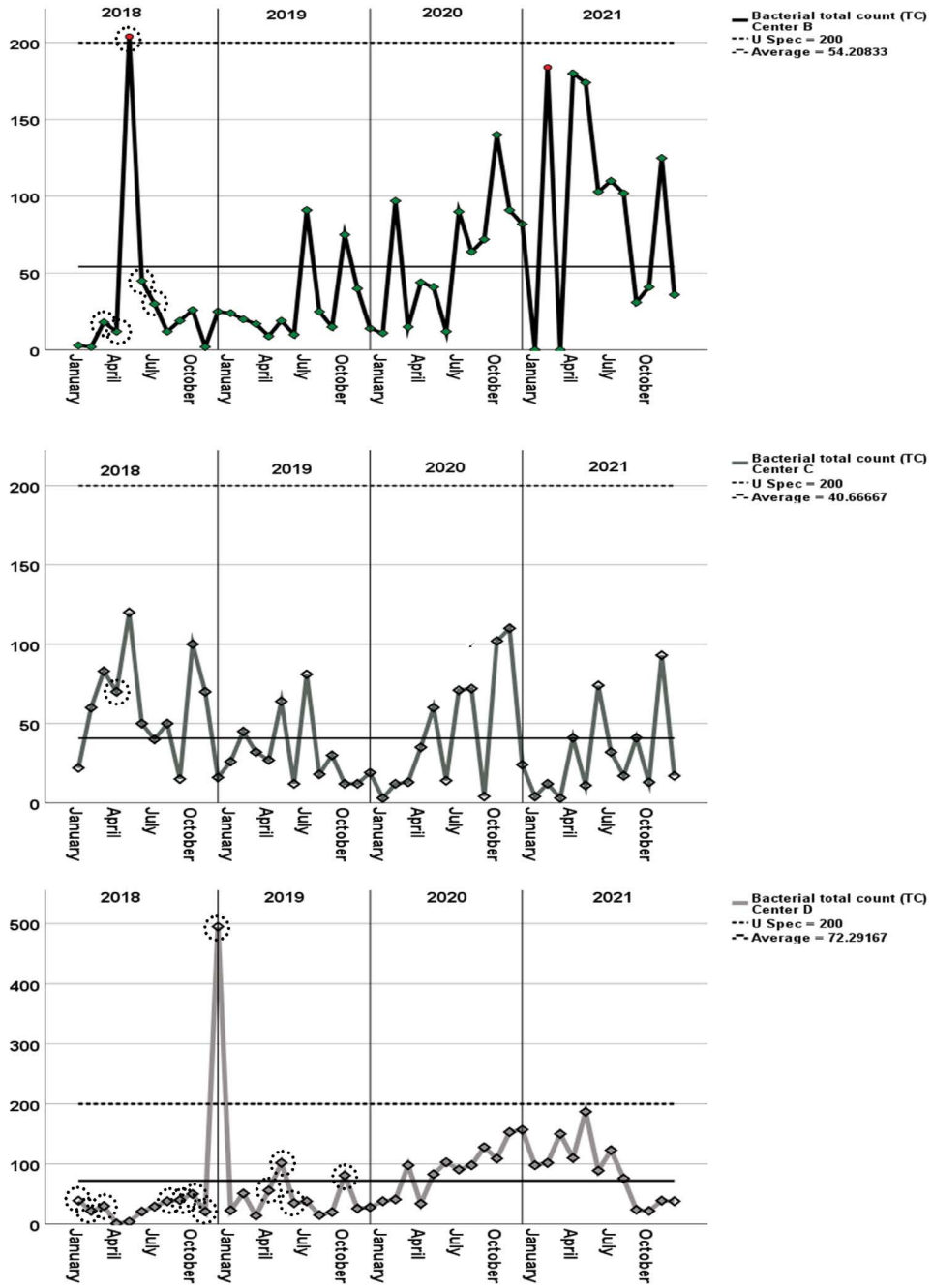


Fig. 3. Charts represent the total bacterial count of Hemodialysis centers. The circles show the points where Pseudomonas aeruginosa was detected.

implemented. The elevated heterotrophic bacterial counts and the growth of *P. aeruginosa* in centers B and D were detected due to water stagnation in the outlet from RO systems and the formation of biofilms in the dead ends at the final inlet of water to the dialysis machine.

As the water system could hardly be changed, applying chemical disinfection protocols or ozone treatment in addition to microbial monitoring of the dialysis water and distribution system are important measures to prevent biofilm formation [25,26]. Disinfection and sterilizing protocols for dialysis units and water distribution systems are carried out by using (hydrogen peroxide and peracetic acid). This disinfection treatment is performed every 40 d with 2 h of contact time to disinfect the water distribution system. To ensure complete sterilization of the water system, additional ozone treatment is performed for 1 h of contact time. The current study evaluated disinfection protocols and water microbiological tests of water over 4 y, the effectiveness of applying control measures in hemodialysis centers were also studied. Our findings for centers B and D showed that

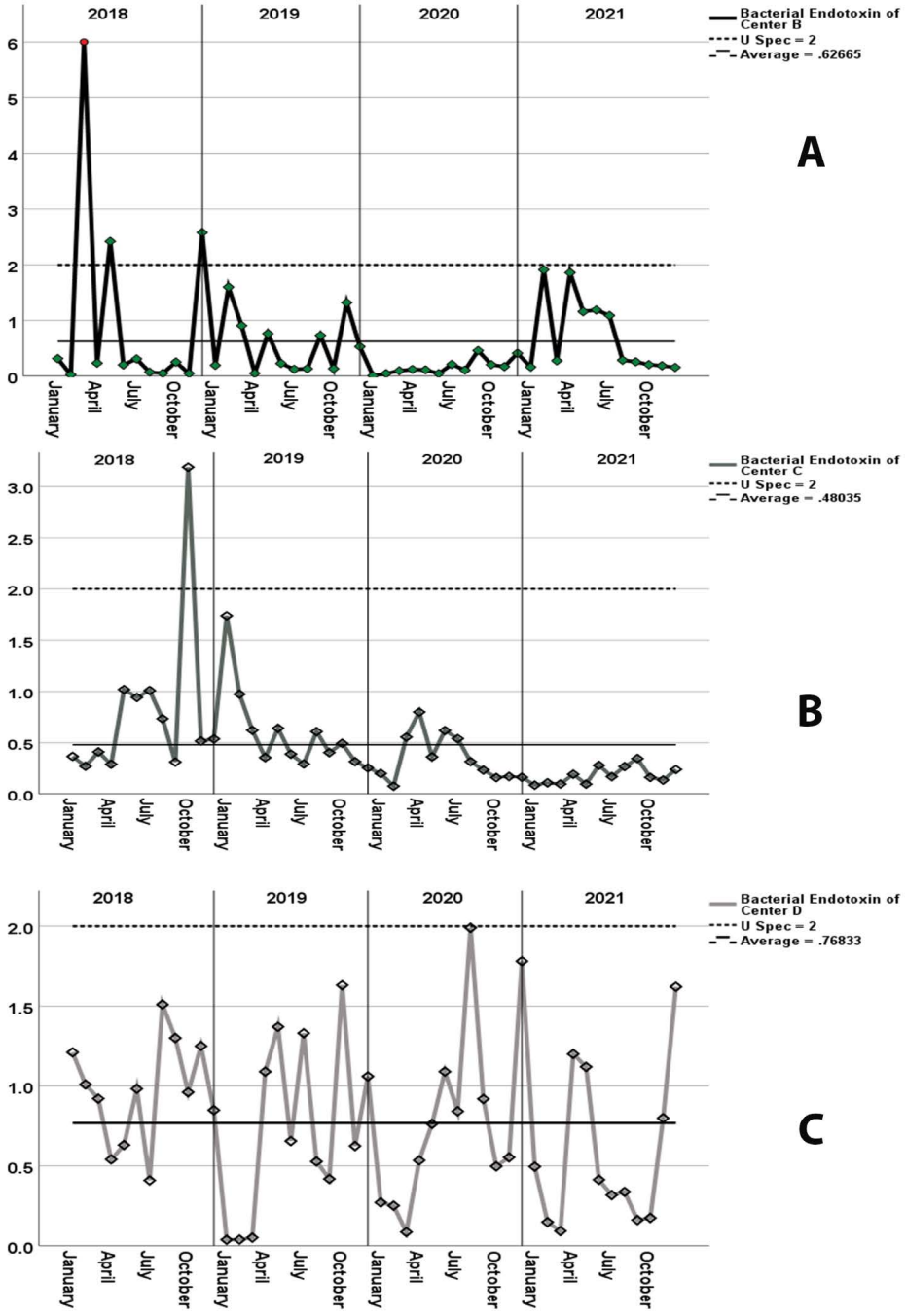


Fig. 4. Charts represent the bacterial endotoxin of Hemodialysis centers.

the growth of *P. aeruginosa* indicated its resistance to the disinfection process. The reasons for such contamination could be linked to different factors, water flow in the system was slow, in addition, there was a stagnation of water in parts of the water system. This resistance of *P. aeruginosa* to disinfection process suggests using a different dosage of disinfectant (higher concentration), or a longer contact time especially when use ozone disinfection which effectively destroys the bacterial cell membrane and degrades endotoxins resulting in bacterial cell lysis [27–30]. Although most contamination incidences were reported in 2018 and 2019, they were not reported in the following years, indicating effective corrective actions were implemented. However, some worrisome of microbiological results were detected afterward, where the results were slightly below the specification limits in centers B and D.

Our study suggested that continual monitoring of microbiological water quality in hemodialysis centers is essential. The applied protocols of the water safety plan and sterilizing disinfectants by hemodialysis centers in hospitals and

thus contribute to the prevention of hospital-acquired infections and improve the quality of the water in the dialysis units. Periodic disinfection of all elements in the water system is necessary to maintain good water quality. If the criteria are not met, testing should be performed every week until the issue is resolved.

Although renal failure patients are at higher risk due to the occurrence of biofilms in water systems, hemodialysis machines could be a reason to contribute to further bacterial exposure. It was found that the chemical disinfection of the hemodialysis machine is partially active on sessile microorganisms. Therefore, biofilm prevention remains the goal to ensure the water quality of hemodialysis treatment. Early recognition of any signs of contamination exceeding the microbial standards requires updating the quality control management, especially the monitoring system. This will require effective awareness, and discipline to record and report microbiological results in logs that allow technicians or supervisors to track chemical, bacterial, and endotoxin data trends. The data should gather the current results associated with these previous testing results in this study and then perform trend analysis to detect any violations of the trends or if the levels are increasing using suitable analytic tools. This will offer prior knowledge if there is either a potential degradation of the water treatment system, an ineffective disinfecting process, or a change in the water source. Hemodialysis centers must be proactive in taking corrective action, such as machine maintenance. Action levels should be established as a level (e.g., 100 CFU/mL for TC, 1 EU/mL for BE) when additional measures must be taken to correct the potential source before the maximum contamination levels have been exceeded and to remain in compliance with the AAMI standards.

During COVID, restricted guidelines and approaches to prevent and control COVID-19 infection were carried out in dialysis centers. These approaches were concerned with pandemic mitigation techniques (e.g., distancing the patients, testing, efficient utilization of medical supplies, and infection serologic evidence) rather than updating the monitoring system or applying a new strategy for preventing contamination of the hemodialysis water system [15,17]. Therefore, the mean BE results before and within the COVID pandemic were comparable in centers B and D. However, the mean results of TC in centers B and D during COVID (2020–2021) were higher than their mean before COVID, especially compared to their data in 2019. This may alarm that the preventive approaches during pandemics should not overlook the importance of proactive measures to prevent potential contaminations of dialysis water, since COVID-19 is particularly harmful to patients on in-center hemodialysis. Therefore, it is recommended to describe these measures in standard operating procedures (SOPs) to be easily followed and controlled.

## 4. Conclusions

The water supply to the hemodialysis units should be monitored frequently. To achieve such a bacteriological quality of dialysis water, several steps are required; this includes applying of physical indicators such as monitoring the water flow within the filtration units, removing the possible bending and dead points within the piping that lead to biofilm formation, placing proper sampling points along with the piping system, in addition to the use of proper chemical disinfection procedures. All of these should be within the SOPs and comply with the quality assurance protocols. As well as effectively written quality control protocols, useful application and implementation of the safety action plan. The goal is eventually to improve the technology of dialysis water and the long-term protection of dialysis water quality according to international standards.

## Availability of data and material

Further supporting material is available upon reasonable request from the corresponding author.

## Competing interests

The authors have no conflict of interest to declare.

## Authors' contributions

N.A. performed all the experiments, K.S. and NA helped in the data analysis and discussion the results, YG revised the initial draft of the MS and revised the MS, and all authors contributed to the writing and approved the final MS.

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