RESEARCH

PERITONITIS AMONG PATIENTS WITH CHRONIC KIDNEY DISEASE UNDERGOING PERITONEAL DIALYSIS

PERITONITES EM PACIENTES COM INSUFICIÊNCIA RENAL CRÔNICA EM TRATAMENTO DE DIÁLISE PERITONEAL

PERITONITIS EN PACIENTES CON INSUFICIENCIA RENAL CRÓNICA EN TRATAMIENTO DE DIÁLISIS PERITONEAL

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ABSTRACT

Objective: Analyze peritonitis rates in the Peritoneal Dialysis Service of a university hospital and identify the profile of patients attending the peritoneal dialysis program. Methods: This observational, retrospective, and descriptive study with a quantitative approach was conducted at a dialysis service in the interior of São Paulo, Brazil, from January to December 2015. Results: Of the 39 patients on peritoneal dialysis, 51.3% were men; 64.1% were non-elderly patients; 51.3% were from towns other than where the service was located; 69.2% were retired; 66.7% were in continuous ambulatory peritoneal dialysis; the duration of treatment of 43.6% ranged from one to two years; 79.5% were not on the transplant waiting list; and 41% had recently started therapy. Of the 20 patients presenting peritonitis, 50% had two episodes and 20% of the episodes were caused by Staphylococcus aureus. The antibiotic was administered intravenously in 90% of the patients; antibiotics were associated with ceftazidime, vancomycin or cephalothin (the most common ones) in 95%. Among those who dropped out of therapy (90%): 65% were women, 55% lived in the same town as the health facility; 70% were retired; 65% were undergoing continuous ambulatory peritoneal dialysis, and were aged 56 years old on average, while treatment duration was 1.7 years on average. The peritonitis rate among those on continuous ambulatory peritoneal dialysis and automated peritoneal dialysis was 2.79%, while 13.33% were on intermittent peritoneal dialysis. Conclusion: Most patients with peritonitis were women, lived in the same town as the facility, were retired and underwent continuous ambulatory peritoneal dialysis, and treatment duration was 1.7 years on average, and 90% of the patients dropped out of therapy.

Keywords: Peritoniti; Peritoneal Dialysis; Renal Insufficiency, Chronic.

RESUMO

Objetivo: analisar a taxa das peritonites no Serviço de Diálise Peritoneal de um Hospital-Escola e conhecer o perfil dos pacientes do programa de diálise peritoneal. Metodologia: estudo observacional, descritivo, retrospectivo, de natureza quantitativa, realizado no serviço de diálise no interior de São Paulo de janeiro a dezembro de 2015. Resultados: dos 39 pacientes em diálise peritoneal, 51,3% eram do sexo masculino, 64,1% não idosos, 51,3% procediam de outros municípios, 69,2% aposentados, 66,7% estavam em diálise peritoneal ambulatorial contínua, 43,6% estavam em tratamento de um a dois anos e 79,5% não estavam na lista de transplante, sendo 41% em virtude de início recente na terapia. Dos 20 pacientes que apresentaram peritonite, 50% tiveram dois episódios no ano, 20% causados por Staphylococcus aureus. Em 90% o antibiótico foi administrado por via endovenosa, 95% tiveram associação de antibióticos, sendo os mais comuns ceftazidima, vancomicina e cefalotina. Dos 90% dos pacientes que saíram da terapia, 65% eram do sexo feminino, 55% moravam no município da instituição de tratamento, 70% eram aposentados e 65% estavam em diálise peritoneal ambulatorial contínua, com média de idade de 56 anos (DP=14,6 anos) e média de 1,7 ano de tratamento. A taxa de peritonite em diálise peritoneal ambulatorial contínua e diálise peritoneal automatizada foi de 2,79% e em diálise peritoneal intermitente 13,33%. Conclusão: a maioria dos pacientes que teve peritonite eram mulheres. A média de peritonites foi maior entre as pessoas com menos idade e menos tempo de tratamento e 90% dos pacientes saíram da terapia.

Palavras-chave: Peritonite; Diálise Peritoneal; Insuficiência Renal Crônica.

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RESUMEN

Objetivo: Analizar la tasa de peritonitis en el servicio de diálisis peritoneal de un hospital escuela; conocer el perfil de los pacientes del programa de diálisis peritoneal. Metodología: Estudio observacional, descriptivo, retrospectivo, cuantitativo realizado en el servicio de diálisis de un hospital del interior del estado de São Paulo, entre enero y diciembre de 2015. Resultados: De los 39 pacientes en diálisis peritoneal, 51,3% eran varones, 64,1% no ancianos, 51,3% venían de otros municipios, 69,2% jubilados, 66,7% en diálisis peritoneal continua ambulatoria, 43,6% en tratamiento entre uno v dos años,79,5% no estaban en la lista de trasplantes y, entre ellos, 41% habían reiniciado recientemente el tratamiento. De los 20 paciente que presentaron peritonitis, 50% tuvieron dos episodios en el año, 20% causado por Staphylococcus aureus. En 90%, el antibiótico se administró vía venosa, 95% tuvieron asociación de antibióticos, siendo los más comunes ceftazidima, vancomicina y cefalotina, y 90% de los pacientes interrumpieron la terapia, 65% eran mujeres, 55% vivían en el municipio de la institución de tratamiento, 70% eran jubilados y 65% estaban en CAPD con promedio de 56 años de edad y 1,7 años de tratamiento. La tasa de peritonitis en diálisis peritoneal continua ambulatoria y diálisis peritoneal automatizada fue de 2,79% y en diálisis peritoneal intermitente 13,33%. Conclusión: Entre los pacientes con peritonitis, la mayoría eran mujeres, el promedio de peritonitis fue mayor entre las personas más jóvenes y con menos tiempo de tratamiento y 90% de los pacientes interrumpieron el tratamiento. Palabras clave: Peritonitis; Diálisis Peritoneal; Insuficiencia Renal Crónica.

INTRODUCTION

Chronic kidney disease (CKD) is characterized by the progressive and irreversible loss of renal function.¹ The kidneys are responsible for filtrating blood, controlling water volume, and producing hormones. When these organs are damaged, their functions are compromised and the main symptoms include edema in the lower limbs, difficulty controlling high pressure, and the significant release of protein in the urine.2 Usually, chronic kidney diseases are caused by primary diseases such as diabetes mellitus, hypertension, and glomerulonephritis, among others.1

Reaching the terminal stage or 5-D stage, when glomerular filtration is less than 10 mL/min/1.73 m² and the introduction of renal replacement therapy (RRT) is required, is a feared situation. RRT is currently available in three modalities: hemodialysis, peritoneal dialysis, and kidney transplantation.² With the exception of kidney transplantation, both hemodialysis and peritoneal dialysis aim for the same purpose. In peritoneal dialysis, the peritoneum comes into contact with the dialysis cleansing fluid that promotes the filtration of undesirable substrates and excess water from the blood.3

There are three ways to perform peritoneal dialysis: continuous ambulatory peritoneal dialysis (CAPD), automated peritoneal dialysis (APD), and intermittent peritoneal dialysis (IPD). In the case of CAPD, the patient uses a closed and manual system, in which the fluid enters and leaves the abdominal cavity by the force of gravity. Normally, three or four exchanges are required per day. APD is performed during the night by a machine (a cycler) that automatically delivers and drains the cleansing fluid. IPD, in turn, is generally performed in a hospital setting and lasts from 20 to 24 hours, on average, and occurs twice a week.4

Regardless of the method chosen, patients need to be properly and clearly instructed because they are responsible for their own care and are more autonomous than patients with other conditions.5

A survey conducted in Brazilian dialysis centers from 2011 to 2013 reveals that less than 10% of chronic kidney patients undergo CAPD, APD or IPD.6 This fact may be associated with a lack of nephrologists and trained nurses and also a lack of health policies and financial support to this type of treatment.⁶

One of the most frequent complications related to peritoneal dialysis is called peritonitis.7 2010 guidelines on peritoneal dialysis-related infections note that 18% of mortality caused by infection is related to peritonitis.8 Peritonitis is the inflammation of the membrane that recovers the organs of the abdominal cavity and the abdomen's internal wall. This membrane is resistant to infections, but infection is common in peritoneal dialysis because of intense manipulation. Peritonitis is the primary cause of therapy dropout or increased morbidity and mortality among patients and is also associated with a higher frequency of catheter removal.¹⁰ For this reason, identifying and controlling cases of peritonitis is key to minimizing occurrences of such an event and improving prevention. This paper's objective was twofold: analyze the rate of peritonitis in the Peritoneal Dialysis Service of a university hospital and identify the profiles of patients attending the peritoneal dialysis program.

METHODS

This observational, descriptive and retrospective study with a quantitative approach was performed in a Nephrology Service in the interior of São Paulo, Brazil. Epidemiological surveillance forms from the Hospital Infection Control Committee (HICC) were used to verify the rate of peritonitis. The database at the nephrology service was used for the analysis of sociodemographic data and the electronic medical records of the patients attending the peritoneal dialysis program were consulted to collect clinical information.

The total sample comprised 331 patients undergoing dialysis in a university hospital from January to December 2015; 292 patients undergoing hemodialysis were excluded. Thirtynine patients receiving peritoneal dialysis were included in the sociodemographic and clinical analysis, while the 20 patients who presented peritonitis in the period were included in the analysis of peritonitis. Note that this study's limitations include the fact that the National Health Surveillance Agency (ANVISA) recalled 38 lots of peritoneal dialysis fluid bags in 2015 due to contamination by a bacterial endotoxin.

The script used to collect data addressed the following variables: demographic data – sex, age, address, occupation, date the RRT was initiated, type of dialysis, whether the patient was on the São Paulo Interior Transplants (SPIT), that is, on the transplant waiting list; and clinical data – episodes of peritonitis, causative microorganisms, treatment implemented, and outcome. Data concerning peritonitis rates were provided by the university hospital's HICC. The formula used to calculate the rate of peritonitis in patients undergoing CAPD and APD was:

X 100 (%)

Number of patients undergoing APD or CAPD in a month

While the rate of peritonitis in patients undergoing IPD was calculated by:

X 100 (%)

Number of patients undergoing IPD in a month

Data were double-entered and validated in MS-Excel® 2010 and later analyzed by the Statistical Package for the Social Sciences (SPSS) version 21.0 using descriptive and inferential statistics. Correlations were verified using Spearman's coefficient of correlation and the Wilcoxon test for paired samples with non-normal distribution was used to compare the means. Correlation and comparison scores were considered statistically significant when p<0.05.

Because this study used only electronic medical records and databases, the Institutional Review Board at FAMERP waived free and informed consent forms. It also approved the study's project according to Resolution 466/12, National Council of Health (Protocol No. 1,650,203).

RESULTS

The nephrology service at the university hospital had 331 patients undergoing dialysis in 2015: 292 on hemodialysis and 39 on peritoneal dialysis (PD). The 39 patients receiving PD presented the following sociodemographic characteristics: ages from seven to 78 years old, 53.5 years old on average (SD = 15.0). Most were men (n=20; 51.3%), non-elderly individuals (n=25; 64.1%), living in neighboring towns (n=20; 51.3%); and retired (n=27; 69.2%) (Table 1).

In regard to the patients' clinical variables, patients undergoing CAPD for one to two years were more prevalent. The duration of PD ranged from four months to 9.3 years, with 1.7 years on average (SD=1.5 year). Thirty-one (79.5%) out of the total pa-

tients on dialysis were not on the transplant waiting list for the interior of São Paulo; 16 (41%) of these were not enrolled because they had only recently started the therapy, as shown in Table 2.

Table 1 - Sociodemographic data of individuals undergoing peritoneal dialysis in the dialysis unit of a university hospital. São José do Rio Preto/SP, Brazil 2015

Sociodemographic variables	n	%		
Sex				
Male	20	51.3		
Female	19	48.7		
Age group				
Non-elderly individuals	25	64.1		
Elderly individuals	14	35.9		
Origin				
Neighboring towns	20	51.3		
São José do Rio Preto - SP	19	48.7		
Occupation				
Retired	27	69.2		
Employed	7	17.9		
Homemaker	4	10.3		
Unemployed	1	2.6		
Total	39	100		

Table 2 - Clinical variables of individuals undergoing peritoneal dialysis in a dialysis unit of a university hospital. São José do Rio Preto/SP, Brazil, 2015

Clinical variables	n	%			
Type of dialysis					
CAPD¹	26	66.7			
APD ²	11	28.2			
IPD ³	2	5.1			
Duration of treatment					
From four months to one year	12	30.8			
From one to two years	17	43.6			
More than two years	10	25.6			
Enrolled in the SPIT4					
No	31	79.5			
Yes	8	20.5			
Reason for not being on the transplant					
Enrolled	8	20.5			
Had only recently initiated treatment	16	41.0			
Age	5	12.8			
Heart disease	4	10.3			
Other	6	15.4			
Total	39	100			

¹⁻ Continuous ambulatory peritoneal dialysis; 2- Automated peritoneal dialysis;

³⁻ Intermittent peritoneal dialysis.

Out of the 39 individuals undergoing peritoneal dialysis at the time of this study, 20 (51.3%) had peritonitis. Table 3 presents these individuals' peritonitis-related variables. Ten (50.0%) of these presented two episodes of peritonitis in 2015, two (10.0%) presented negative culture of the peritoneal fluid, and the remaining presented 14 types of bacteria in the culture of the peritoneal fluid; the most incident was *Staphylococcus aureus* (n=4; 20.0%).

Table 3 - Peritonitis-related variables among individuals undergoing peritoneal dialysis in the dialysis unit of a university hospital. São José do Rio Preto/SP, Brazil 2015

Peritonitis-related variables		%			
Number of peritonitis episodes					
One episode	4	20.0			
Two episodes		50.0			
Three episodes	4	20.0			
Four episodes	2	10.0			
Result of peritoneal fluid culture					
Negative culture	2	10.0			
Klebsiella oxytoca	1	5.0			
Enterobacter aerogenes	1	5.0			
Serratia marcescens	1	5.0			
Staphylococcus haemolyticus	3	15.0			
Staphylococcus epidermidis	2	10.0			
Staphylococcus aureus	2	10.0			
Staphylococcus hominis	1	5.0			
Staphylococcus spp.	1	5.0			
Staphylococcus viridans	1	5.0			
Staphylococcus capitis and Staphylococcus hominis	1	5.0			
Staphylococcus viridians and Staphylococcus mitis	1	5.0			
Pseudomonas fluorescens and Trichosporon asahii	1	5.0			
Staphylococcus epidermidis and Staphylococcus aureus	1	5.0			
Staphylococcus aureus and Proteus mirabilis	1	5.0			
Use of ATB¹ in the treatment of peritonitis					
In the dialysis bag	2	10.0			
Intravenous	10	50.0			
In the dialysis bag and intravenous	8	40.0			
ATBs² used in the peritonitis treatment					
Ceftazidime and cephalothin	5	25.0			
Ceftazidime; cephalothin and vancomycin		20.0			
Ceftazidime; cephalothin; vancomycin and ciprofloxacin		5.0			
Ceftazidime; cephalothin; vancomycin and meropenem		5.0			
Ceftazidime; cephalothin and fluconazole		5.0			
Ceftazidime and vancomycin		10.0			
Ceftazidime; vancomycin and ciprofloxacin	1	5.0			

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Table 3 - Peritonitis-related variables among individuals undergoing peritoneal dialysis in the dialysis unit of a university hospital. São José do Rio Preto/SP. Brazil 2015

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Peritonitis-related variables		%			
ATBs ² used in the peritonitis treatment					
Ceftazidime; vancomycin; cefepime; ampicillin	1	5.0			
Ceftazidime; vancomycin and levofloxacin		5.0			
Ceftazidime; vancomycin and rocefin		5.0			
Ceftazidime; vancomycin and meropenem		5.0			
Vancomycin		5.0			
Outcome of peritonitis treatment					
Terminated peritoneal dialysis	18	90.0			
Replaced the Tenckhoff catheter		5.0			
Septic shock		5.0			
Total		100			

1- Antibiotic; 2- Antibiotics

In regard to peritonitis treatment, 18 (90.0%) individuals were administered intravenous antibiotics accompanied or not by antibiotics in the dialysis bag and 19 (95%) individuals received associated antibiotics. The most frequently used were ceftazidime, vancomycin, and cephalothin. In 18 (90%) cases, the patients had to drop out of the PD treatment.

Most of the 20 individuals with peritonitis were women (n=13; 65.0%); lived in São José do Rio Preto – SP (n=11; 55.0%); were retired (n=14; 70.0%); and were undergoing CAPD (n=13; 65%). Ages ranged from 19 to 78 years old, 56.0 years old on average (SD=14.6 years), while duration of their peritoneal dialysis treatment ranged from four months to three years, with 1.7 years on average (SD=1.0 year).

Associations among the variables of 39 individuals undergoing peritoneal dialysis were analyzed using Spearman's coefficient of correlation. Statistically significant association was found between sex and the occurrence of peritonitis (coefficient=0.33; p=0.43), indicating that women presented more episodes of peritonitis than men. No association was found between the occurrence of peritonitis and the variables: address, occupation, age, type of treatment, or duration of treatment. The Wilcoxon test, however, revealed that the average number of peritonitis cases was greater among younger individuals (p=0.00) whose duration of treatment was shorter (p=0.00).

The patients attending the PD program in the automated and continuous ambulatory modalities presented an average rate of peritonitis of 2.79% a year, while patients undergoing intermittent dialysis presented a rate of 13.33%.

In regard to peritonitis rates, the greatest difficulty reported by the HICC was to gather data on peritonitis because re-

lated information was not clearly and systematically recorded in the patients' medical records or in a specific spreadsheet.

DISCUSSION

One of this study's limitations is the sample size. Data are in agreement with those the Brazilian Society of Nephrology reported based on their 2015 survey, in which 91.4% of chronic kidney patients undergoing dialysis were on hemodialysis.¹¹

The sample included 39 patients, a number explained by the reduced number of patients attending the PD program at the university hospital under study. In regard to sociodemographic data, patients were 53.5 years old on average (SD=15.0 years), a result that is similar to that found in a study conducted in a center for the treatment of kidney diseases located in Bahia, Brazil, in which the patients' average age was 54.6 years old.¹²

Most individuals in the sample were men (51.3%), data that corroborate the 2015 survey conducted by the Brazilian Society of Nephrology, which reports that 58% of the patients undergoing dialysis in Brazil are men.¹¹ Another study conducted in a specialized service located in São Paulo found a similar result, specifically that 68% of the population were also men.¹³

In regard to age, non-elderly individuals predominated (64.1%); ages ranged from seven to 59 years old. This finding is similar to that reported by a study conducted in the state of São Paulo, in which most patients (56%) in the sample were aged between 18 and 59 years old.¹³

Most patients in this study lived in a town other than where the hospital at which they received treatment was located (51.3%). This information differs from that found in a study conducted in five facilities located in Mato Grosso do Sul, Brazil where most patients (54.3%) lived in the same town as their treatment facility.¹⁴ The main reason a patient chooses a given type of PD is the possibility of keeping elements of their lives, such as jobs and social lives, and the type that facilitates adaptation to the treatment. The fact that the health service was located in another town is one of the potential reasons most patients opted for PD, that is, to be able to perform the therapy at home and to decrease the number of visits paid to the health facility.¹⁵

Even though one of the benefits of PD is the possibility to keep one's job, in this study 69.2% of the patients were retired. This information diverges from a study conducted in Jequié, Bahia, in which 52.5% of the individuals were retired. This context is not exclusive to this population, because a study conducted in Italy revealed that 32.1% of the participants were retired and 27.8% were unemployed. The same study stresses that 48.4% of the patients quit working after having initiated RRT. 16

In regard to clinical data, the CAPD modality predominated (66.7%). Such a finding is also reported by a study conducted in Ribeirão Preto, SP, Brazil, in which 53.7% of the par-

ticipants also underwent CAPD.¹⁷ This information differs from that reported in the Brazilian literature, as the 2015 census conducted by the Brazilian Society of Nephrology reports that of a total of 45,073 patients undergoing RRT in Brazil, most of those undergoing peritoneal dialysis opted for APD (5.0%) and only 2.0% opted for CAPD.¹¹

The duration of treatment found in this study ranged from one to two years (43.6%). This finding is similar to that found in a study conducted in Porto Alegre, RS, Brazil, which indicated that the duration of treatment among 60% of the patients was below two years.¹⁸

Of the 39 patients, 79.5% were not on the transplant waiting list, and the reason reported by 41% of these was that they had only recently initiated the treatment, 1.7 years ago on average. This context is similar to that reported by a study conducted in Belo Horizonte, MG, Brazil in which patients took 1.7 years on average to get added to the list.¹⁹

In regard to the 20 cases of peritonitis that occurred during the study period, most patients had at least two episodes in the year (50%). This result is similar to that found by a study conducted in Rio Grande do Sul, in which 27.2% of the patients had experienced one episode of peritonitis and 17.8% had had two episodes of peritonitis in the study period.²⁰

In 20% of the peritonitis cases, *Staphylococcus aureus* was present in most cultures of the peritoneal fluid. This is similar to that found by a study conducted in the São Lucas Hospital, located in Porto Alegre, in which 19.8% of the cases had been caused by *Staphylococcus aureus*. ²⁰ The International Society of Peritoneal Dialysis (ISPD) guidelines report that *Staphylococcus aureus* and *Pseudomonas aeruginosa* are the most common microorganisms in exit-site and tunnel infections and are the ones most frequently related to peritonitis. ²¹

In 90% of the cases, patients treated the infection intravenously, with and without association with intra-peritoneal antibiotics therapy. The updated guidelines published by the International Society of Peritoneal Dialysis in 2016 recommend maintaining intra-peritoneal (IP) administration as first choice, except among patients with sepsis. IP dosage results in high local levels of antibiotics.²¹ The context verified in this study is explained by the fact the hospital under study does not have an IP antibiotics therapy protocol.

In this study, 95% of the patients had more than one antibiotic associated with the treatment and the most frequently used were ceftazidime, vancomycin and cefazolin. A meta-analysis conducted in a state university in Botucatu, SP, Brazil did not find a superior therapeutic regimen among those investigated, though a better response was obtained when gly-copeptide was used in combination with ceftazime.²²

The main outcome in 90% of the cases in this study was PD dropout. According to international guidelines updated in 2010,

less than 4% of cases result in death, so that death is not the main outcome of peritonitis. The most common outcome is peritoneal membrane failure, caused by repeated exposure to infection.²³

Among the 20 patients who presented episodes of peritonitis, 65% were women and 65% were undergoing CAPD. These results are in agreement with those reported in a sample studied in Porto Alegre, in which 63% were women and 69% were undergoing CAPD. One potential explanation for such a finding is the high likelihood of women experiencing hemoperitoneum during their menstrual cycle. The average duration of treatment was 1.7 years, a finding similar to that reported by a study conducted in Sergipe, showing that 32.2% of the sample was undergoing treatment from one to three years and 30% were in the first year of PD.²⁴

A total of 55% of the sample lived in the same town where their health facility was located. This information is similar to that reported by a study addressing patients with chronic kidney disease from Juiz de Fora, MG, in which 64.6% of the patients lived in the same town as their treatment facility.²⁵

In this sample, 70% of those who had peritonitis were retired. A study conducted in two facilities located in Ribeirão Preto reports that 62.2% of the patients who participated in that study were retired. This result is found among most chronic kidney patients because the treatment often impedes the individual from working, as s/he becomes unable to meet the work demands imposed by companies.¹⁷ In this study, the Wilcoxon test revealed that peritonitis more frequently affected younger individuals (p=0.00), with treatments having a shorter duration (p=0.00), in contrast with the findings of a study conducted in the northeast of Brazil, in which most patients who experienced peritonitis were elderly individuals with two or more years of treatment.²⁴

In regard to the rate of peritonitis, the Infection Control Committee calculates the rate and sent data to those responsible for epidemiological surveillance. The rate of peritonitis in APD and CAPD cases was 2.79%, while among those undergoing IPD, it was 13.33%. The IPD rate was high due to the small number of patients in this modality; only one individual was on IPD at the time, so that one episode of peritonitis considerably raised the rate. According to the ISPD, it is expected that rates will not exceed one episode every 18 months (0.67/year at risk), though rates also depend on the size of the population considered. The ISPD also recommends peritonitis cases be monitored and compared with the rates reported in the literature.^{21,23}

CONCLUSION

Statistically significant association was found between sex and the occurrence of peritonitis, showing that women presented peritonitis more frequently than men. No associations were found between peritonitis and address, occupation, age, type of treatment, or duration of treatment, although the average number of episodes of peritonitis was higher among younger individuals with shorter duration of treatment. This study's limitations include its time frame and local context. Note that in 2015, the National Health Surveillance Agency (ANVISA) collected 38 batches of peritoneal dialysis fluid bags due to contamination by bacterial endotoxin. These results reinforce the need for further research to complement these findings in order to support and improve the work of multidisciplinary teams in the prevention and treatment of this occurrence.

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