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Original Article

Cost Analysis of Hospital Treatment for Peritoneal Dialysis-Associated Peritonitis

Milorad Stojadinovic [1], ****Radica Zivkovic Zaric*** [2,3], ***Dejan Petrovic*** [4,5], ***Aleksandra Kezic*** [1,6], ***Milan Radovic*** [1,6], ***Svetlana Jovicic Pavlovic*** [1], ***Ivana Mrdja*** [1], ***Lara Hadzi Tanovic*** [1], ***Violeta Knezevic*** [7,8], ***Dejan Pilcevic*** [9,10], ***Tamara Jemcov*** [6,11], ***Marija Karapandzic*** [11], ***Slobodan Jankovic*** [2,3]

1. *Department of Nephrology, University Clinical Center Serbia, Belgrade, Serbia*
2. *Department of Pharmacology and toxicology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia*
3. *Department of Clinical pharmacology, University Clinical Center Kragujevac, Kragujevac, Serbia*
4. *Department of Nephrology, University Clinical Center Kragujevac, Kragujevac, Serbia*
5. *Department of Internal Medicine, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia*
6. *Department of Internal medicine, Medical Faculty, University of Belgrade, Belgrade, Serbia*
7. *Department of Nephrology, University Clinical Center Vojvodina, Novi Sad, Serbia*
8. *Department of Internal medicine, Medical Faculty, University of Novi Sad, Serbia*
9. *Department of Nephrology, Medical Military Academy, Belgrade, Serbia*
10. *Department of Internal Medicine, Medical faculty of the Military Medical Academy, University of Defense in Belgrade, Serbia*
11. *Department of Nephrology, General Hospital Zemun, Belgrade, Serbia*

***Corresponding Author:** Email: radica_zivkovic@yahoo.com

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Abstract

Background: Increasing healthcare spending is a significant issue, with the aging population contributing to a rise in patients needing renal replacement therapy. The cost of peritoneal dialysis (PD) is substantial, particularly in upper-middle-income countries like Serbia. We aimed to identify the direct costs and influencing factors of treating peritoneal dialysis-associated peritonitis (PD associate peritonitis) in Serbia.

Methods: A retrospective observational study was conducted on consecutive patients admitted due to PD-associated peritonitis in five tertiary care hospitals across Serbia in 2019-2022. The primary outcome was total cost of hospitalization. Potential predictors were determined using generalized linear model with a gamma probability distribution and a log link function.

Results: The study included 122 patients. The average total cost per patient was 1131.90±1538.67 USD, with the cost of hospitalization (348.17 ± 361.52 USD) and antibiotics (294.94±465.88 USD) being the most significant. The length of hospitalization (P<0.001) and treatment outcome (P<0.001) were found to be significant predictors of the total cost.

Conclusion: The costs of treating PD associate peritonitis in Serbia are substantial, with each additional day of hospitalization significantly increasing the cost. The importance of patient and doctor education about infection prevention is underscored by the health consequences and the lengthy, expensive treatment when an infection occurs.

Keywords: Peritoneal dialysis; Peritonitis; Costs

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Introduction

Increasing healthcare spending represents a significant contemporary issue. Estimates indicate that since the 1950s, the average annual increase in healthcare spending in the UK has been 3.7%, a rate that is notably higher than annual economic growth. It is expected that the aging of the population will continue this trend (1). The aging population also promotes an increase in the number of patients with end-stage kidney disease who are in need of kidney replacement therapy, with projections for 2030 exceeding 5.5 million people worldwide (2). Furthermore, the annual cost of peritoneal dialysis (PD) is substantial and varies between countries, ranging from 4,000 to 91,000 USD. On average, in upper-middle-income countries like Serbia, it is around 14,500 USD. (3)

Cost-of-illness studies are designed to quantify socioeconomic costs associated with a particular disease, including those related to any comorbidity that may develop over time. This allows for the potential savings to be calculated in case of successful disease prevention. All costs can be categorized into three groups:

- Direct costs, which include both healthcare and non-healthcare expenses. Healthcare costs encompass diagnostic procedures, treatment, rehabilitation, etc., while non-healthcare costs cover aspects such as transportation, relocation, legal expenses.
- Indirect costs, associated with the loss of labor productivity due to illness. (4)
- Non-material expenditures, defined as the suffering and pain of patients, i.e., the deterioration of quality of life. (5)

Peritoneal dialysis as one of modalities of kidney replacement therapy, offers certain advantages over hemodialysis. It is the preferred treatment for some patients, especially those who have heart issues and cannot have vascular access created. Additionally, patients on PD tend to preserve residual kidney function somewhat longer than those on hemodialysis. However, PD-associated peritonitis is a leading cause of morbidity and mortality in these patients (6). The rate of peritonitis varies significantly between countries, ranging from 0.06 episodes per year in Taiwan to 1.66 episodes per year in Israel. Interestingly, these differences can be observed even within the same country. This condition can lead to further complications, such as the need for extraction of the PD catheter, relapses, and a potential transfer to hemodialysis (7), further increasing the cost. A study on pediatric patients in the United States estimated that the average cost of peritonitis treatment is around 13,000 USD (8). However, the factors associated with the costs of hospital treatment for peritonitis in peritoneal dialysis patients have not been investigated in detail.

This study aimed to identify the direct costs and the factors influencing these costs when treating this complication in an upper-middle-income country like Serbia. Given that nothing similar has been done in Balkan countries, the advantage of our study is that it was done in several different centers in the central Balkan state of Serbia. This would be important because we can compare our research with developed countries and see where we are in terms of the way we treat patients with peritoneal dialysis-associated peritonitis.

Methods

Study design and population

This retrospective observational study was carried out on a series of consecutive patients admitted due to PD-associated peritonitis in five tertiary hospitals across Serbia from Jan 1, 2019, to Dec 31, 2022. These hospitals include the University Clinical Center Serbia (UCCS), University Clinical Center Kragujevac, University Clinical Center Vojvodina, Clinical Hospital Center Zemun, and the Military Medical Academy. The patient population was selected based on the criteria of being over 18 yr old and having a diagno-

sis of PD-associated peritonitis. Patients with incomplete records, died in first 24 hours or those transferred to another department for further treatment were excluded from the study. We took data from the medical documentation and avoided selection bias because all patients with peritoneal dialysis associate peritonitis were included in the analysis.

The UCCS Ethics Committee approved the study (approval number 1177/9, dated December 12, 2022), conducted in line with the ethical principles of the World Medical Association Declaration of Helsinki for medical research involving human subjects.

Data Collection

Data were gathered from electronic medical records and included information such as gender, age, weight, primary kidney disease, duration of PD treatment, type of PD, history of peritonitis, peritonitis incidence rate, comorbidities, Charlson Comorbidity Score, class of the isolate in the PD culture, length of hospital stay, treatment outcome, number of ECGs, morphological diagnostics, consultative examinations, type of drugs and number of doses used for peritonitis treatment, number of erythrocyte concentrate transfusions, and laboratory analyses (microbiological, hematological, biochemical).

The official pricing for diagnostic investigations and treatment was obtained from the Republic Fund of Health Insurance of the Republic of Serbia. The average official middle exchange rate of the Serbian dinar against the US dollar was 108.5 according to the National Bank of Serbia in Feb 2024 (9). Primary outcome of study was total cost of hospitalization.

Statistical analysis

A minimum sample size sufficient to determine factors significantly associated with total cost of treatment was calculated using G-Power (10). The assumed cost size and its variability were taken from a similar study (11): 0.05 probability of type 1 error, power of the study 0.80. The calculated sample size was 85 patients.

Data obtained from the information systems were first numerically coded, tabulated, and checked for errors. Data were then described by measures of central tendency and variability (if continuous) or by frequencies and relative numbers (percentages). Mean, median, standard deviation, and interquartile range described the distribution of the data. The effects of independent variables on the study outcome were analyzed by generalized linear model with a gamma probability distribution and a log link function. The goodness of fit for the model was assessed using the Pearson Chi-square statistic and the Omnibus test. Results were considered statistically significant if the probability of the null hypothesis was 0.05 or less.

All analyses were performed using the IBM SPSS Statistics for Windows, ver. 23.0 (IBM Corp., Armonk, NY, USA).

Results

Overall, 122 patients who met the inclusion criteria were enrolled in the study. The patients' mean age was 61.3 ± 15.52 yr, and 53 (43.4%) of them were male. Hypertension and/or diabetes mellitus were the primary causes of end-stage kidney disease (ESRD) in 61 (50%) of the patients. The average duration of PD before the onset of peritonitis was 36.7 ± 36.2 months. The baseline characteristics of the study group are summarized in Table 1.

The average length of hospitalization was 24.5 ± 25.4 d. During this period, patients received an average of 73.6 ± 57.3 doses of antibiotics and 4.1 ± 9.9 doses of antimycotics. The associated costs were as follows: length of hospitalization - 348.17 ± 361.52 USD, antibiotic - 294.94 ± 465.88 USD, and antimycotic treatments- 72.95 ± 558.18 USD. Utilization of healthcare resources and costs are presented in Table 2.

Table 1: Characteristics of the study sample (n = 122)

Variable		Value (mean ± SD, median, [IQR]) or count (%)
Age		61.3 ± 15.2, 65.0 [21.0]
Sex (male/female)		53 / 69 (43.4% / 56.6%)
Body weight (kg)		68.2 ± 16.3, 69.5 [20.3]
Diabetes mellitus (yes/no)		38 / 83 (31.4% / 68.6%)
Main cause of renal failure	HTA	34 (27.9%)
	DM	17 (13.9%)
	Both HTA and DM	10 (8.2%)
	Glomerulonephritis	21 (17.2%)
	Hereditary	6 (4.9%)
	Infectious	2 (1.6%)
	Unknown	32 (26.2%)
Time on peritoneal dialysis (months)		36.7 ± 36.2, 25.5 [38.0]
Number of previously treated peritonitis		1.1 ± 1.4, 1.0 [2.0]
Isolated microorganisms from peritoneal fluid	Gram-positive	57 (46.7%)
	Gram-negative	18 (14.8%)
	Candida sp.	2 (1.6%)
	Nothing isolated	45 (36.8%)
Treatment outcome: survived/died		111 / 11 (91.0% / 9.0%)
Charlson's comorbidity index		5.2 ± 2.0, 5.0 [2.0]

SD – standard deviation; IQR – interquartile range; HTA – hypertension; DM – Diabetes mellites;

Table 2: Utilization of healthcare resources and costs (mean ± SD, median, [IQR])

Variable	Utilization (number)	Costs (USD)
Length of hospitalization (days)	24.5 ± 25.4, 18.0 [12.0]	348.17±361.52, 256.31[174.44]
Specialists' encounters	2.2 ± 3.2, 1.0 [3.0]	5.64±8.36, 2.62[7.85]
Microbiological analyses	3.6 ± 2.4, 3.0 [2.0]	25.60±20.54, 22.65[19.40]
Full blood counts	14.8 ± 17.8, 9.0 [11.0]	39.52±38.35, 27.19[27.19]
Biochemical tests	82.1 ± 83.8, 59.0 [58.0]	209.10±236.44, 139.39[149.14]
ECGs	2.1 ± 3.4, 1.0 [1.0]	11.83±19.07, 5.53[5.53]
Radiological diagnostic procedures *	1.6 ± 1.9, 1.0 [2.0]	23.51±33.33, 7.34[27.81]
Disposable syringes, needles and infusion sets used	151.6 ± 181.3, 112.0 [151.0]	27.50±32.38, 21.51[26.98]
Doses of antibiotics	73.6 ± 57.3, 56.0 [67.0]	294.94±465.88, 126.05[266.98]
Doses of antimycotics	4.1 ± 9.9, 0.0 [0.0]	72.95±558.18, 0[0]
Doses of other drugs	33.9 ± 61.8, 16.0 [38.8]	43.21±105.99, 2.81[29.99]
Erythrocyte transfusions	0.5 ± 1.4, 0.0 [0.0]	7.74±20.53, 0[0]
Replacing peritoneal catheter	0.1 ± 0.3, 0.0 [0.0]	5.29±13.68, 0[0]
Temporary hemodialysis	0.2 ± 0.4, 0.0 [0.0]	4.35±9.32, 0[0]
Total	N.A.	1131.90±1538.67, 638.19[738.67]

* Radiological diagnostic procedures: ultrasound examinations, computerized tomography, nuclear magnetic resonance or X-rays

The generalized linear model with log link and gamma distribution was used to analyze the relationship between several independent variables and the main outcome, i.e., the total costs. The independent variables included in the model were: sex, diabetes mellitus, previous infection of PD catheter, Charlson comorbidity index, treatment outcome, age, time on PD before onset of peritonitis, number of previous peritonitis, and length of hospitalization. The model has satisfactory fit to the data with Pearson Chi-square value of 14.069, and a p-value of 0.174. All assumptions were met. Overall model was statistically significant with the Omnibus test value of 167.292, with a *P*-value<0.001. Significant predictors were presented in Table 3.

Table 3: Results of the generalized linear model (Pearson Chi square 14.069, P=0.174; omnibus test 167.292, P<0.001). Dependent variable: total costs. Variables included in the model: (Intercept), sex, diabetes mellitus, previous infection of peritoneal catheter, Charlson comorbity index, treatment outcome, age, time on peritoneal dialysis before onset of peritonitis, number of previous peritonitis, length of hospitalization. Probability distribution gamma, link function log.

Predictor	B ± 95% CI	*P*
Length of hospitalization	0.037 ± 0.032	<0.001
Treatment outcome (died/survived)	-0.485 ± 0.245	<0.001

CI – confidence interval

Discussion

Major findings of our study confirmed that the direct cost of hospital treatment for PD-associated peritonitis significantly contributes to the overall cost of PD treatment. This highlights the importance of our study in clarifying the additional costs of treating peritonitis from a pharmacoeconomic perspective. The length of hospitalization has a positive correlation with total costs, while, conversely, death as an outcome has a negative correlation with total costs.

Previous studies from Spain and Colombia, which included patients with peritonitis associated with peritoneal dialysis, showed a predominance of males with an average age of 56.7 yr as well as study from Germany; they studied the effect of gender on peritoneal dialysis (12-14). In comparison, our patient group is slightly older (61.3 ± 15.52 yr) and has a higher prevalence of females. In general, there are more women in the population, so it makes sense that more women have a problem with peritonitis associated with peritoneal dialysis. In the USA, women are 12% more likely to initiate PD than men (15). Furthermore, they have almost twice the chance of getting peritonitis (16), which supports our findings. In our study, hypertension and diabetes mellitus were the primary causes of end-stage kidney disease (ESRD) in 61 (50%) of the cases. These are the main causes of chronic kidney failure in high and middle-income countries (17). However, this differs from a Spanish study that reported glomerulonephritis (22.7%) as the most common cause, followed by diabetic nephropathy (19.8%). Generally, when we look at surrounding countries we have similar results to Greece, where hypertension, and cardiovascular diseases followed by diabetes mellitus are the most common cause of PD (18). Before the first episode of peritonitis, the average duration of PD was about three years per patient

The average length of hospitalization for patients in our study was 24.5±25.4 d, with associated costs of 348.17±361.52 USD. These findings are similar to a study from Colombia, which reported an average hospitalization duration of 22.2 d (13). In our study, the primary cost drivers for perito-

nitis treatment were antibiotics (294.94±465.88 USD) and antimycotics (72.95±558.18 USD). These results align well with the Colombian study (13). When we consider results from the USA, we can conclude that they had higher pharmacy treatment costs (1191 USD) (19). This is likely due to the fact that the USA and other high-income countries have registered medicines that are more expensive compared to those on the Serbian market (20). Our results point out great variability when antimycotics are used. When we used agents from the imidazole group, the costs were lower compared to echinocandins, where the price was much higher.

The most commonly isolated microorganisms from peritoneal fluid were gram-positive microorganisms, as in other studies (21,22). A significant portion of the funds also went towards biochemical analyses (209.10±236.44 USD).

Some patients do not require hospitalization. According to the International Society for Peritoneal Dialysis, the decision to admit a patient to the hospital depends on several factors. These include the patient's hemodynamic status, the severity of their symptoms, the treatment schedule selected for automated PD patients, the feasibility of administering intraperitoneal antibiotics on an outpatient basis, and the patient's compliance (23).

Generally, the total cost per patient amounts to 1131.90±1538.67 USD. This value is significantly lower when compared to the treatment costs in the USA, but significantly higher when compared to the costs in Colombia (13,17). Such a result is expected because the USA is more developed than Serbia and other Balkan countries, and also because the costs of healthcare services (bed-day, encounter with a specialist, diagnostic examinations, etc.) are much higher and not regulated administratively, like in Serbia (24).

The length of hospitalization positively correlates with the total cost of peritonitis treatment. The longer a patient stays in the hospital, the higher the cost. This is because each additional day in the hospital incurs extra costs, including the cost of therapy. In most cases, a patient stays longer in the hospital due to the need for extended antimicrobial therapy. On the other hand, death as an outcome has a negative correlation with total costs. This implies that when a patient's hospital stay is shortened due to death, the treatment costs are reduced. The costs of treating peritonitis are substantial, particularly given that Serbia is a medium-developed country with average monthly gross earnings of 1,214 USD (25). These costs would probably be higher, but due to the pandemic, some patients supposed to be hospitalized were admitted on an outpatient basis

Our study has several limitations. Firstly, we only included direct costs as we had access solely to patients' medical histories. Additionally, some patients were transferred to different departments for treatment of other accompanying diseases. This made it impossible to precisely segregate the cost of peritonitis treatment from other treatments, especially for patients who continued antimicrobial treatment. Therefore, we excluded those patients. Finally, our study was conducted during the COVID-19 pandemic, have affected the treatment outcomes of some patients.

Conclusion

Each additional day of hospitalization significantly increases the cost, therefore more efficacious treatments with shorter hospital stays could be drivers of substantial savings. Additionally, patients with less severe symptoms, who are younger, more compliant, have fewer comorbidities, and live near the clinic, should be considered for outpatient treatment to reduce treatment costs. It is certainly recommended that these facts be noticed by the competent authorities who would issue specific recommendations for the treatment of this group of patients. In addition, these conclusions probably could be applied to the most of the Balkan countries, especially the countries of the former Yugoslavia (e.g., North Macedonia, Bosnia and Herzegovina, Montenegro etc.).

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or

falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Conflict of interest

The authors declare that there is no conflict of interests.

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