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# Medical problems in patients with chronic kidney disease undergoing hemodialysis and their therapy

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## Abstract:

**Background:** It was reported that hemodialysis (HD) with either a new or reused dialyzer raises medical problems that require therapeutic regimens. This study aimed to investigate the medical problems and their management in patients undergoing HD.

**Methods:** This study was conducted by prospectively observing patients with chronic kidney disease undergoing HD. The incidence of medical problems and the treatment given were recorded.

**Results:** Among 351 cases of HD, medical problems occurred in 15.7% of cases, including hypotension as the most dominant, followed by muscle cramps, shivering, headache, asphyxia, fever, chest pain, and pruritus. Hypotension was ameliorated with intravenous 40% dextrose and normal saline. Muscle cramps were overcome with 40% dextrose, normal saline, methampyrone, and calcium gluconate. Shivering was managed by warming the patients followed by intravenous methampyrone, 40% dextrose, and normal saline. Meanwhile, headache was reduced by paracetamol or intravenous methampyrone and 40% dextrose. Fever was treated by intravenous methampyrone or oral paracetamol. Pruritus was managed by intravenous dexamethasone and diphenhydramine.

**Conclusions:** Medical problems occurring during HD are prevalent and need immediate therapy. Pharmacists and clinicians should work in collaboration to improve the patients' quality of life.

**Keywords:** chronic kidney disease, drug-related problem, hemodialysis, medical problems

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## Introduction

The global prevalence of chronic kidney disease (CKD) is increasing. In developing countries, the prevalence of CKD is estimated to be about 40–60 cases per million population [1]. Nephrology centers in Indonesia, for example, reported that the prevalence of CKD ranged between 200 and 250 cases per million population [2]. Moreover, patients with stage IV CKD need renal replacement therapy, and one of the options is hemodialysis (HD). Although the use of HD has been progressing worldwide, many patients still experience medical problems related to the HD process, such as hypotension, muscle cramps, nausea, vomiting, headache, chest pain, back pain, and shivering [3]. Thus, this study was conducted to investigate the prevalence of medical problems in patients with CKD undergoing HD treatment. Furthermore, we examined the therapeutic management and potential drug-related problems. This study is expected to support the improvement of drug utilization and anticipatory strategies for medical problems caused by HD.

## Materials and methods

This study was conducted from April 10 to June 16, 2010, by prospectively observing patients with CKD undergoing HD treatment in the Haemodialysis Unit of Dr. Soetomo General Hospital Surabaya. The inclusion criteria were stage 4 or 5 CKD that requires HD with or without medical problems related to the HD process.

**Budi Suprpti** is the corresponding author.

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## Results

A total of 351 HD cases fulfilled the inclusion criteria of the study. Among the 351 cases, 54 medical problems occurred. The medical problems included hypotension (5.9%), muscle cramps (2.9%), chills (2.6%), headache (1.4%), shortness of breath (1.4%), fever (0.6%), chest pain (0.3%), and itching (0.3%) (Table 1). The managements for hypotension, muscle cramps, shivering, and headache are shown in Table 2–Table 5, respectively. In this study, we also observed whether or not a new dialyzer or a reused dialyzer resulted in different medical problems (Table 6).

**Table 1:** Medical problems that occurred during HD.

Types of medical problem	Frequency	Percentage, % <sup>a</sup>
Hypotension	21	5.9
Muscle cramps	10	2.9
Chills	9	2.6
Headache	5	1.4
Shortness of breath	5	1.4
Fever	2	0.6
Chest pain	1	0.3
Itching	1	0.3
Total number of medical problems	54	15.4

<sup>a</sup>Percentage to total HD cases.

**Table 2:** Therapeutic management for hypotension.

Therapeutic intervention	Dose	No. of patients
D40 i.v. + NaCl 0.9 i.v.	D40, 25–100 mL; NaCl 0.9, 100–250 mL	10
D40 i.v.	D40, 25–75 mL	11
Total		21

D40, 40% dextrose.

**Table 3:** Profile of therapeutic management for muscle cramps induced by HD in patients with CKD.

Therapeutic intervention	Dose	No. of patients
D40 i.v.	25–50 mL	2
D40 i.v. + NaCl 0.9 i.v.	D40, 25 mL; NaCl, 200 mL	2
D40 i.v. + Ca gluconate i.v.	D40, 75 mL; Ca gluconate 10%, 10 mL	1
Decreasing UF rate		1
Decreasing UF + D40 i.v. + NaCl 0.9 i.v.	D40, 25 mL; NaCl, 50 mL	1
Methampyrone oral	500 mg	3
Total		10

UF, Ultrafiltration.

**Table 4:** Profile of therapeutic management for shivering induced by hemodialysis in patients with CKD.

Pharmacological therapy/intervention	Dose	Non-pharmacological therapy	No. of patients
Paracetamol peroral	500 mg	Lamp + blanket	1
Methampyrone peroral	500 mg		2
Methampyrone peroral	500 mg	Lamp + blanket	3
		Lamp + blanket	2
D40 i.v.	25 mL	Lamp + blanket	1



D40 i.v. + NaCl 0.9 + methampyrone	D40, 25 mL; NaCl, 100 mL; methampyrone, 500 mg	Lamp + blanket	1
Total			10

**Table 5:** Profile of therapeutic management for HD-induced headache in patients with CKD.

Therapeutic intervention	Dose	No. of patients
Paracetamol + diphenhydramine i.v.	Paracetamol, 500 mg; diphenhydramine, 10 mg	1
Paracetamol peroral	500 mg	3
Methampyrone	500 mg	1
Total		5

**Table 6:** Profile of medical problems related to the use of new/reused dialyzer for patients with CKD.

Types	No. of medical problems		Percentage, % <sup>a</sup>	
	New	Reused	New	Reused
Hypotension	3	18	4.7	6.3
Shivering	–	10	–	3.5
Muscle cramps	2	7	3.1	2.4
Headache	3	2	4.7	0.7
Shortness of breath	–	5	–	1.7
Fever	–	2	–	0.7
Chest pain	–	1	–	0.3
Itching	–	1	–	0.3
Total	8	46	12.5	15.9
Total dialyzer	64	287		

<sup>a</sup>Percentage to total HD cases.

## Discussion

Hypotension was the most prevalent medical problem caused by HD, occurring in as much as 5.9%. This is in accordance with a previous research report showing that the prevalence may range from <5% to 40% of all HD cases [4]. Hypotension during HD is thought to occur mainly due to changes in relative blood volume that theoretically has a great impact on blood pressure. Agustriadi et al. has shown the relationship between changes in relative blood volume and an episode of intradialytic hypotension [5]. It is stated that there is a strong and notable relationship between changes in relative blood volume and episodes of intradialytic hypotension. It is reported that a 1% change in relative blood volume increases the risk of hypotensive episodes by 35%. Other factors such as type of dialysate, anemia, use of antihypertensive drugs, diabetic condition, humoral factors, nitric oxide, and various cytokines may also contribute to hypotension events [5].

In the present study, the therapy for hypotension during HD consisted of intravenous 40% dextrose and 0.9% NaCl (Table 2). The infusion of 0.9% NaCl acts by increasing the plasma volume, cardiac output, and blood pressure [6]. Meanwhile, 40% dextrose acts not only by adding intravascular volume but also as a hyperosmolar fluid that draws water from extravascular compartments into the intravascular lumen, in turn increasing the plasma volume, cardiac output, and blood pressure [6]. It is known that there are methods to treat hypotension caused by HD. The patient is placed in the Trendelenburg position prior to the immediate infusion of normal saline at a volume of  $\geq 100$  mL, if needed. Hypertonic saline, glucose, mannitol, or albumin solution may be used to replace 0.9% NaCl. If cramps occur, hypertonic saline may be needed. Provision of nasal oxygen may be useful in maintaining myocardial function [7].

The present study revealed that muscle cramps appeared in 2.9% of patients undergoing HD. Muscle cramps probably occurred due to changes in muscle perfusion caused by ultrafiltration during HD [8]. The present study showed that all patients with muscle cramps were administered with intravenous 40% dextrose, normal saline, methampyrone, and calcium (Ca) gluconate (Table 3). Forty percent dextrose and normal saline

increased the intravascular volume, thus directly improving blood flow to the muscle. Methampyrone 500 mg/mL injection relieves the acute pain due to muscle cramps, and Ca gluconate is administered as a calcium supplement for hypocalcemia [9].

The data showed that shivering occurred in 10 patients (3.5%), which might be caused by pyrogenic reaction due to endotoxin. Endotoxin is a lipopolysaccharide with a large molecular weight and is released through the outer membrane of gram-negative bacteria. Endotoxin is most likely derived from the dialysate fluid or dialyzer contaminant that passes through dialyzer membranes into the blood. Shivering was overcome by exposing patients to a sodium lamp and covering their body with a blanket to provide warmth. Paracetamol 500 mg was also orally given (Table 4). Intravenous administration of methampyrone, infusion of 40% dextrose, and normal saline were given for conditions that coincide with shivering.

In addition, headache occurred in five patients (1.6%). Headache during HD is a manifestation of suspected imbalance syndrome or disequilibrium syndrome. The therapy that followed the headache symptom during HD was oral paracetamol 500 mg and intravenous methampyrone 500 mg (Table 5). The other therapy administered for conditions that accompany headache was 40% dextrose, which is commonly administered to increase the intravascular volume and vascular tension [6]. Further, intravenous diphenhydramine administration was used. Antihistamine administration is suggested to overcome allergies experienced by patients undergoing HD [10].

The study results showed that shortness of breath occurred in patients during HD. This medical problem occurred in five patients (1.4%). There are several causes of shortness of breath, such as air embolism during catheter placement. The air flow into the pulmonary arteries may cause shortness of breath accompanied by chest pain, cyanosis, and cough [8]. In addition, the residues of peracetic acid on the dialyzer may cause shortness of breath, cough, headache, nausea, and vomiting due to the damage in mucous membranes and upper respiratory tract [11]. Our present data showed that nasal oxygen delivery was given for patients experiencing shortness of breath during the HD process.

Pyrogenic reactions that occurred during the HD process caused fever in two patients. The therapies used to treat fever were methampyrone 500 mg administered intravenously and acetaminophen 500 mg administered orally. Meanwhile, chest pain occurred in one patient. It is known that mild chest pain, which is usually accompanied by mild back pain, occurs in 1%–4% of HD cases. It might be caused by the decrease in blood flow due to ultrafiltration flow in blood vessels including the cardiac blood vessels. In the present study, ultrafiltration was utilized in patients developing chest pain during HD.

The present study found that medical problems might occur in association with a new or reused dialyzer (Table 6). It was found that hypotension was more prevalent with the use of a reused dialyzer. It is possible that the event caused by allergy to peracetic acid was due to the reuse of the dialyzer [12]. However, the incidence of shivering, muscle cramps, itching, fever, and headache was higher with the use of a new dialyzer. Nevertheless, the total incidence of medical problems was higher with the use of a reused dialyzer as compared to that of a new one. The reuse process can lead to changes in pore size, thus increasing the chance of entry of bacteria or viruses through the dialyzer membrane pore into the patient's bloodstream and causing various medical problems [12].

## Conclusions

This study indicated that medical problems experienced by patients undergoing HD are common. The therapy may vary depending on the symptoms that appear. The role of the clinical pharmacist is important to help clinicians improve the patients' quality of life.

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**Author contributions:** All of the authors contributed to the design of the study, the acquisition and interpretation of the data, and critical revision of manuscript. All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

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**Informed consent:** Informed consent was obtained from all individuals included in this study.

**Ethical approval:** Research involving human subjects complied with all relevant national regulations, institutional policies and is in accordance with the tenets of the Helsinki Declaration (as revised in 2013), and has been approved by the authors' institutional review board (46/Panke.KKE/11/II/2010).

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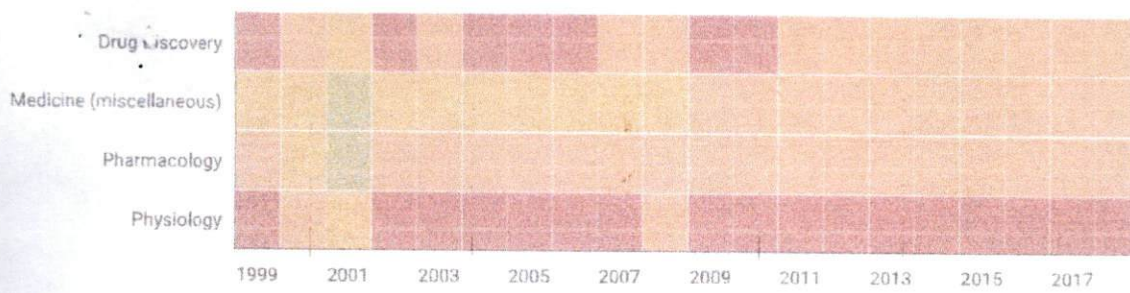
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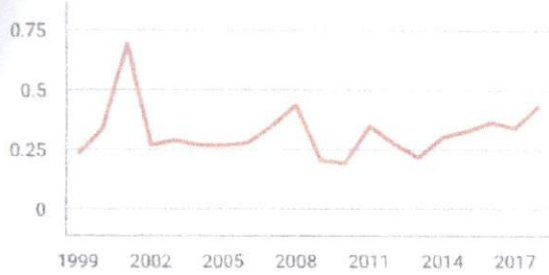
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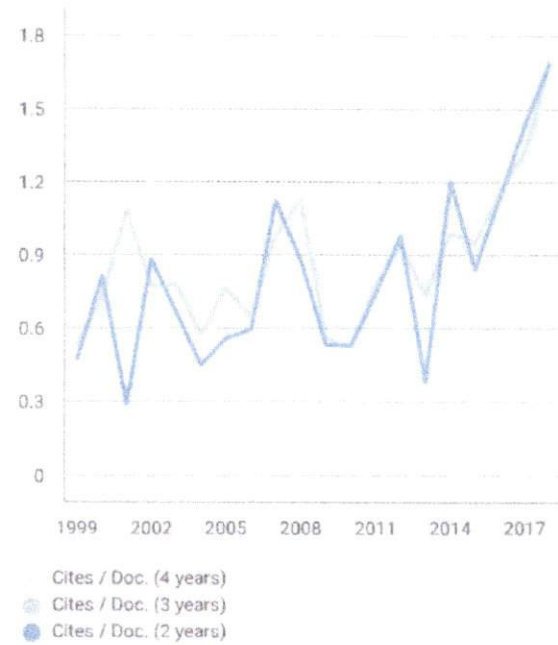
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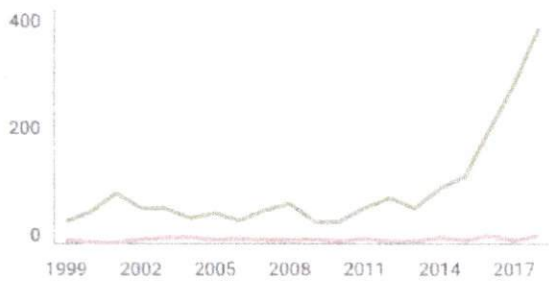
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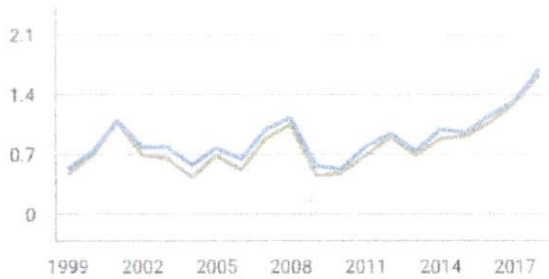
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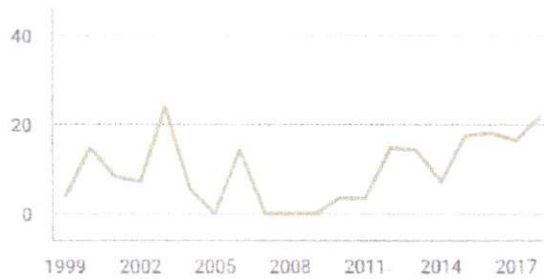
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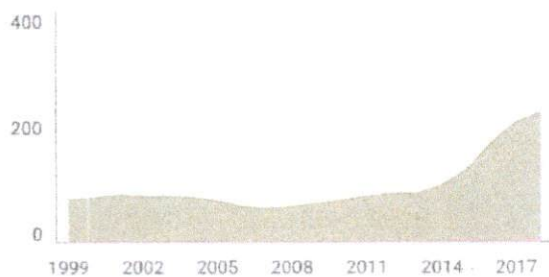
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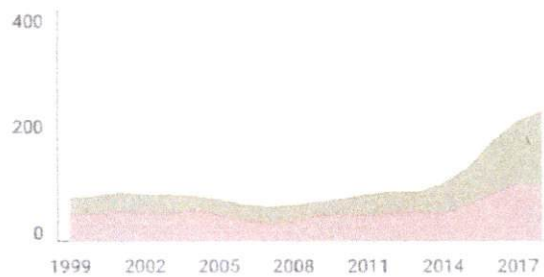
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