



RESEARCH ARTICLE

Prevalence and comorbid for late-stage chronic kidney disease (CKD) in patients undergoing continuous ambulatory peritoneal dialysis (CAPD) due to urinary obstruction

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Abstract

Chronic Kidney Disease (CKD) is a condition of gradual or chronic decline in kidney function, which is quite severe and caused by various kidney diseases, including urinary obstruction. This disease is progressive and generally irreversible. CKD requires kidney replacement therapy, one of which is continuous ambulatory peritoneal dialysis (CAPD). To determine the prevalence and risk factors for End Stage Renal Disease (ESRD) in patients undergoing CAPD due to urinary obstruction. We performed a retrospective cohort with a cross-sectional study was conducted using secondary data from medical record data of ESRD patients with CAPD accompanied by urinary obstruction at Dr. Saiful Anwar General Hospital, Malang, Indonesia. The prevalence of CKD in patients with CAPD accompanied by urinary obstruction was 6,50% and dominated by males (57,8%) with an age range of 41-50 years (26%). The majority of comorbidities are severely high the Body Mass Index (BMI) (89,0%) and hypertension (80,8%). The location of obstruction is mostly unilateral (5,64%) with mild levels (4,06%). Urinary obstruction is a frequent clinical finding in CKD patients with CAPD. The most common risk factor in this study was hypertension. The prevalence and comorbidities among CAPD patients with Urinary obstruction (UO) are better understood because to this study. It is necessary to recognise its limitations, particularly the small sample size and single-centre design. Future studies should involve more centres and larger patient groups in order to provide a more thorough knowledge of the mechanisms behind the high survival rates among CAPD patients.

1. INTRODUCTION

Chronic Kidney Disease (CKD) is a condition marked by a gradual decline in kidney function due to various renal diseases. It is a progressive and usually irreversible condition (1). According to the Kidney Disease Improved Global Outcome (KDIGO) definition, CKD is a kidney structure or function abnormality that persists for more than 3 months and has health implications, as indicated by cause, glomerular filtration rate (GFR) category and albuminuria (2). CKD can be caused by pre-renal, renal, and post-renal factors. Pre-renal issues refer to anything

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affecting the kidney's condition before entering its anatomy such as hemodynamic, etc. Renal pertains to parts within the kidney itself, while post-renal involves parts of the genitourinary system after the kidney, including the channels that leading to the external urethral meatus (3).

Data from the Indonesian Renal Registry (IRR) in 2020 reveals that the prevalence of CKD underlying diseases among dialysis patients is highest in hypertensive kidney disease, followed by diabetic nephropathy and glomerulopathy. Urinary obstruction (UO) is an anatomical or functional obstruction at any level in the urinary tract, including the kidneys, ureters, bladder, and urethra. UO ranks fifth, accounting for 7% of CKD (4,5). However, there is still a lack of evidence regarding the prevalence and comorbidities of CKD patients with UO.

Clinical symptoms of UO can vary among patients, influenced by factors such as the duration from the onset of obstruction to treatment, presence of infection, intrinsic or extrinsic factors causing the obstruction, location of the obstruction (unilateral or bilateral), and partial or total obstruction (6). Acute UO could manifest as colic renal, macroscopic haematuria, gastrointestinal symptoms, fever and chill if accompanied by infection or a burning sensation during urination. The pain is caused by hyperperistaltic muscle in the upper urinary tract from the infundibulum to the distal ureter (7).

UO is frequently found in patients with End Stage Renal Disease (ESRD) or CKD. Obstruction can occur at any point in the urinary tract, leading to renal parenchymal injury. Acute Kidney Injury (AKI) is observed in less than 5% of UO cases. In children, UO accounts for 16% of CKD cases. In older men, prostate conditions are the primary cause of urinary obstruction, contributing to 5% of end-stage renal disease cases. The prevalence of UO in ESRD patients is growing. Each year, around 2000 people with a suspected diagnosis of obstructive nephropathy are initiated on ESRD and 2% of them becoming ESRD patients. Among these patients, 4% are under the age of 20; 44% are between 20 and 64; and the remaining are over the age of 64 (8,9).

The management of ESRD patients involves renal replacement therapy, which may include chronic dialysis or renal transplant. Chronic dialysis methods encompass haemodialysis and peritoneal dialysis, with Continuous Ambulatory Peritoneal Dialysis (CAPD) (10). CAPD involves the placement of a catheter in the peritoneal cavity through either laparotomy or endoscopic surgery, requiring a healthy peritoneal cavity with excellent peritoneal membrane function (11,12). The author's aim is to investigate the prevalence and comorbidities of end-stage CKD in patients with CAPD associated with urinary obstruction, particularly at Dr Saiful Anwar General Hospital Malang.

2. MATERIALS AND METHODS

2.1. Research Design

This study employs a cross-sectional methodology and is non-experimental correlational in nature. The study was a descriptive research design study and used secondary data from medical record data of end-stage CKD patients with CAPD who had UO at Dr. Saiful Anwar General Hospital Malang from August to September 2023. The patients' identity remained confidential during the study, and ethical clearance for the research was obtained from the Health Research Ethics Commission of the Faculty of Medicine, Universitas Brawijaya, Dr. Saiful Anwar General Hospital Malang, with approval number No. 173/EC/KEPK-S1-PD/07/2023.

2.2. Time and Place

This study was conducted at the Hemodialysis Installation of Dr. Saiful Anwar General Hospital Malang for 3 months from the 1st of August to the 31st of October 2023.

2.3. Population and Sample

The population in this study includes end-stage CKD patients undergoing CAPD with UO at Dr. Saiful Anwar General Hospital Malang in 2023. The samples for this study were collected from the medical records of all CKD patients in end-stage CKD patients undergoing CAPD with UO who met the inclusion criteria. Inclusion criteria for this study were end-stage CKD patients undergoing CAPD with UO at Dr. Saiful Anwar General Hospital Malang from August 1st to October 31st 2023 with complete medical record data including gender, age, BMI, comorbidities, obstruction location and duration. Patients with incomplete medical records were automatically excluded from the study.

2.4. Study Variables

The variables in this study included UO patients of both genders. Age variable was divided into seven categories: (a) 10-20; (b) 21-30; (c) 31-40; (d) 41-50; (e) 51-60 years old; (f) 61-70 years old; and (g) older than 71

years old. Comorbidities evaluated included Diabetes Mellitus (DM), Hypertension, and unknown. Obstruction location was categorised as unilateral or bilateral. Body Mass Index (BMI) was divided into categories of severely thin, thin, normal, overweight, and obese. The duration of CAPD was divided into a range of 0-2, 3-5 and more than 5 years.

2.5. Data Analysis

The prevalence data was analysed using univariate test to describe the distribution of the obtained data and to understand their data comprehensively. The foundation of univariate studies is statistical testing, which yields a p-value (the likelihood that the observed difference is the result of chance).

3. RESULTS AND DISCUSSION

3.1. General Characteristics of Patients Undergoing Hemodialysis and Continuous Ambulatory Peritoneal Dialysis (CAPD)

This study aimed to determine the prevalence and comorbidity of end-stage CKD in individuals with CAPD and UO. This study is a form of descriptive research using secondary data, specifically medical records containing information on the patient’s gender, age, BMI, comorbidities, obstruction location and duration of CAPD. The study gathered data from 246 medical records at Dr. Saiful Anwar General Hospital Malang in 2023. Among the 246 medical record data, the most prevalent risk factor was hypertension in 199 patients and 16 patients who experienced UO with the majority being between 41-50 years old and with hypertension being one of the most commonly found risk factors (Table 1).

Table 1. Patients’ characteristic descriptions

Variables	N = 246	Percentage (%)
Genders		
Male	142	57.7
Female	104	42.2
Age		
10-20 years old	15	6
21-30 years old	45	18
31-40 years old	53	22
41-50 years old	64	26
51-60 years old	47	19
61-70 years old	24	9
>71 years old	6	2
Body mass index (BMI)		
Severely Thin	17	6.9
Thin	2	0.8
Normal	6	2.4
Overweight	2	0.8
Obese	219	89
Risk Factors		
DM	36	14.6
Hypertension	199	80.8
Not known	11	5.6
Occurrence of Obstruction		
Duration of CAPD		
0 – 2 years	101	41.1
3 – 5 years	104	42.3
> 5 years	41	16.6

Based on Table 1, indicates a predominance of male patients (57.7%). As per the 2023 *Survei Kesehatan Indonesia* (SKI), According to Indonesia Health Survey (*Survei Kesehatan Indonesia-SKI*) 2023, male is found to be the majority among CKD survivors. Furthermore, the age group of 41-50 years also dominates in this study (26%) followed by group age of 31-40 years old (22%) (13).

The distribution of BMI categories reveals a significant predominance of patients classified as obese with total of 219 patients (89.0%) and only 6 patients within normal weight (2.4%). Hypertension is conspicuous among the findings, identified in 199 patients (80.8%) and marked as the primary risk factor for CKD in UO cases. However, in Indonesia, hypertension and DM both account for the highest number of CKD cases, signifying their status as significant risk factors for urolithiasis, the primary cause of UO. Urolithiasis is known to increase the probability of developing CKD twofold compared to the general population (14,15). The data indicates unilateral obstruction with mild and moderate severity, predominantly characterizes the observed cases of obstruction. The duration of CAPD in patient data found out that the majority of cases comprised 104 patients (42.3%) with 3-5 years of CAPD, followed by 101 patients (41.1%) with 0-2 years of CAPD and 41 patients (16.6%) have been using CAPD for more than 5 years.

Table 2 shows the distribution of ESRD patients with CAPD, 16 patients have UO. Among these patients, that dominated with 14 patients (5.69%) have unilateral UO, while 2 patients (0.81%) have bilateral UO. In unilateral urinary obstruction, the other healthy kidney can maintain renal clearance. This condition can remain asymptomatic, leading many patients to find and seek medical treatment in the terminal stage of CKD. In contrast, patients with bilateral UO experience symptoms earlier, making the condition more noticeable and thus diagnosable at an earlier stage (16).

Table 2. Urinary obstruction (UO) occurrence

Obstruction Locations	n	%*
Unilateral	14	5.7
Mild	10	4.1
Moderate	4	1.6
Severe	0	0
Bilateral	2	0.8
Mild	2	0.8
Moderate	0	0
Severe	0	0
Total	16	6.5

*Percentage among 246 total cases

3.2. CKD and Age

Age is intricately linked to various non-communicable diseases. DM and hypertension are fundamentally characterized by insulin resistance and endothelial dysfunctions, both of which escalate with age. Age-related factors contribute significantly to UO, notably in the kidney. Afflictions such as renal cell carcinoma disease, calculus disease, cystic disease and obstructive pyelonephritis affect the kidney, while the ureter is susceptible to ureteral stricture, calculus disease, transitional cell carcinoma, retroperitoneal malignancy, gynaecological malignancy. Bladder-related conditions encompass bladder neck contracture, neurogenic bladder, bladder and/or prostate malignancy, benign prostatic hyperplasia (BPH), prostatitis and calculus disease. Conditions of the urethra include stricture, meatal stenosis, phimosis and urethral malignancy. Notably, these conditions exhibit a distinct age-related increase in prevalence (17).

In line with the present investigation, the highest incidence of CKD caused by UO occurred among individuals aged 41 and 50. The data revealed that CKD is more prevalent among individuals over 41, highlighting the strong association between age and UO-induced CKD (17). While CKD can develop at any age due to various diseases, it becomes increasingly likely with age. Studies have shown that around the age of 40, renal filtration starts to decline by approximately 1% each year (18). Furthermore, age-related kidney degeneration is compounded by a higher incidence of kidney-damaging afflictions among the elderly, such as diabetes, hypertension, and cardiovascular disease. A 6% prevalence of CKD has been noted among individuals aged 10 to 20, potentially correlating with UO caused by congenital disorders, such as maternal obesity, gestational diabetes, preeclampsia and substance abuse (drug addiction and smoking) (19). Furthermore, the majority of CAPD patients in Malang, East Java, are males aged 46 to 59 (20). Gender is also associated with the progression of CKD. A meta-analysis of thirty studies that stratified data by gender found that CKD progresses faster in men than in women, possibly due to the Reno protective effect of female sex hormones (21).

3.3. CKD and Body Mass Index

In this study, the data indicates that the majority of CKD patients with CAPD were categorized as overweight or obese. The correlation between being overweight or obese and CKD is well-documented with multiple underlying factors. Obesity is a primary cause of CKD and is closely linked to conditions such as diabetes, hypertension, renal hemodynamic changes, as well as structural and histological renal changes. Adipose tissue plays a pivotal role in the production of adipokines, including leptin, adiponectin, monocyte chemoattractant protein-1, tumour necrosis factor- α (TNF- α), transforming growth factor- β (TGF- β), and angiotensin-II.

Impaired insulin sensitivity contributes to the pathophysiological mechanism of renal injury by exacerbating the effects of angiotensin II, escalating proteinuria, and triggering the production of inflammatory cytokines. These conditions lead to mesangial growth, hypertrophy, hypercellularity, and glomerular hyperfiltration. Furthermore, obesity-induced oxidative stress prompts the generation of angiotensin-II within the body, elevates plasminogen activator inhibitor-1 and tumour growth factor (TGF) levels and promotes glomerular fibrosis. As renal fibrosis progresses, the increasing systemic volume load induces glomerular hyperfiltration and hypertension (22).

Both experimental and clinical research have demonstrated that maternal obesity elevates the risk of premature mortality and chronic disorders in children, including obesity, hyperglycaemia, and diabetes. Primary mechanisms among obese patients encompass increased macronutrient intake, epigenetic modifications, dysregulated adipokine production, and persistent inflammation. Evidence suggests that prenatal exposure to maternal obesity increases the probability of late-onset CKD in children, signifying that intrauterine exposure to obese mothers constitutes a notable risk factor for CKD (23,24).

The embryonic kidneys of obese mothers are susceptible to oxidative stress, chronic inflammation, and fibrosis damage, with potential detrimental persisting until adolescence. Clinical studies have revealed that maternal diabetes or obesity increases the risk of children developing conditions such as hypertension, renal hyperfiltration, and chronic kidney disease. A study of 1,994 children with CKD indicated that low birth weight, maternal overweight or obesity, and pre- and gestational diabetes, are factors associated with an elevated risk of childhood CKD. Children exposed to overweight or obese mothers had a 24% to 26% higher risk of developing CKD compared to controls (19,25).

The majority of participants in this study were classified as obese based on their BMI. Irrespective of diabetic status, obese mothers were more likely to have children with CKD caused by UO when compared to non-obese mothers. This evidence indicates that maternal obesity hinders kidney development and raises the risk of CKD in children, potentially attributable to autophagy, chronic inflammation, oxidative stress, or epigenetic regulation (24). Furthermore, environmental factors can also contribute to kidney dysfunction in children born to obese mothers. Additionally, childhood obesity and other comorbid conditions, such as intrauterine growth anomalies and low birth weight exacerbate the negative impact of maternal obesity on the child's kidney function (19).

3.4. Diabetes Mellitus as a Risk Factors of CKD

Type II Diabetes Mellitus is a condition characterised by oxidative stress due to hyperglycaemic conditions. Bladder dysfunction in diabetes is also associated with oxidative stress (26). Studies have found an elevation of oxidative stress in bladder tissue in diabetic patients (27). Oxidative stress markers in urine, such as 8-hydroxy-2'-doxyguanosine, have been utilised as biomarkers for Lower Urinary Tract Disorders (LUTD), including diabetes. Bladder dysfunction is believed to contribute to UO, which has four main causes: inflammatory, neoplastic, inherited, and miscellaneous (28).

Angiotensin II significantly contributes to the pathophysiology of various diseases. Specifically, AT1 antagonists exhibit antihypertrophic effects on diverse tissues, particularly those associated with smooth muscle growth. Bladder outlet obstruction represents the most extensively researched model of bladder hypertrophy, leading to UO and subsequent acute and chronic renal failure (27).

This study revealed that 36 patients (15% of respondents) were diagnosed with diabetes mellitus. While the precise aetiology of CKD is unknown, diabetes mellitus is causally linked to CKD, particularly when attributed to UO.

3.5. Hypertension as a Risk Factors for CKD

In this study, it was found that 199 individuals (80.8%) had hypertension. Uncontrolled hypertension is widely acknowledged as an independent risk factor for chronic renal failure. However, the high proportion of respondents with hypertension was presumed to be linked to secondary hypertension induced by chronic renal

failure. Several factors contribute to the elevation of blood pressure in CKD patients, including neurological and hormonal alterations that disrupt blood pressure regulation (29). CKD has been associated with increased Renin-Angiotensin-Aldosterone System (RAAS) activity. Furthermore, diminished blood flow in the peritubular capillaries of the sclerosed glomeruli triggers renin hypersecretion, leading to elevated angiotensin II levels in the bloodstream. Angiotensin II serves as a direct vasoconstrictor and promotes an increase in systemic vascular resistance and blood pressure. In CKD, the reduced number of functioning glomeruli necessitates the compensatory increase of the glomerular filtration rate (GFR) in the remaining glomeruli. This elevation in perfusion pressure and GFR can be achieved through the increase in systemic arteries pressure (30).

3.6. Urinary Obstruction Location

As per the investigation findings, 6.50% of patients encountered obstruction from up to 16 persons with 4.06% experience dominance of a unilateral site. UO typically appears unilaterally, but can occasionally develop bilaterally, resulting in anuria. The main distinction between unilateral and bilateral obstruction in the initial acute phase (first 1-2 hours) is the glomerular filtration rate (GFR) and renal blood flow (RBF). In unilateral obstruction, RBF is reduced in the affected kidney, while the healthy contralateral kidney maintains a stable GFR during this phase (31,32).

In cases of bilateral obstruction, GFR decreases proportionate to the level of obstruction. The intermediate phase (2 - 5 hours later) is followed by the late phase (24 hours) and the period after the first 24 hours of obstruction. Tubular damage occurs 5 minutes after occlusion due to increased pressure within the tubules. This additional pressure is transmitted to the site of Bowman capsule, causing a decrease in intravascular hydrostatic pressure and GFR. Changes in RBF further reduce GFR. During the acute blockage phase, there is an increase in prostaglandins and prostacyclin due to compression of the arterial network in Bowman's capsule, leading to an initial rise in RBF. This increase is temporary and gradually decreases by up to 50% after 2 hours. The decrease in RBF is caused by an increase in renal vascular resistance due to the presence of vasoconstrictor substances such as thromboxane A2 and angiotensin II. As RBF declines, the pressure in the glomerulus also decreases, leading to a further decrease in GFR (31,32).

Patients with UO commonly experienced changes in distal tubular function. Acute occlusion results in increase reabsorption of sodium by the ducts, leading to a urine sodium concentration of <10 mEq/L and a sodium excretion fraction of <1%, indicating prerenal acute renal failure (33). Continued obstruction causes substantial sodium loss, mainly due to tubule injury and decreased sodium-potassium adenosine triphosphate phosphatase (Na-K ATPase) enzyme activity. Reabsorption of sodium in the distal tubule results in the elimination of hydrogen and potassium. Failure to eliminate hydrogen and potassium in patients with UO results in renal tubular acidosis. Difficulties in reabsorption along the arch of Henle also hamper the distal nephron's ability to efficiently concentrate urine (32).

Elevated intratubular pressure prompts distension of the renal collecting system, with hydronephrosis initially affecting the pelvis and subsequently extending to the calyces. Ischemia and increased pressure in the arcuate arteries, which traverse the base of the renal pyramid, are likely contributors to the renal parenchyma atrophy. As the pressure in the renal collecting system approaches the glomerular filtration pressure (6-12 mmHg), urine output decreases and the kidney ability of concentrating the urine is gradually lost. Residual urine is reabsorbed into interstitial and lymphatic tissues through a process known as pyelointerstitial backflow, allowing a blocked kidney to maintain urine production. Pyelointerstitial backflow, which is caused by contrast flowing backward from the pyramids into the subcapsular tubules in the renal interstitium (the intertubular, extraglomerular, extravascular space of the kidney), only occurs following forniceal rupture (32).

3.7. CKD and CAPD Duration

The study revealed that patients with ESRD undergoing CAPD therapy had a one-year survival rate of 80%, a three-year survival rate of 60%, and a five-year survival rate of 52%, with an average survival duration of 42.4 months. Similarly, research conducted in Hong Kong between 2002 and 2006 found that patients had survival rates of 90.8% at one year, 68.2% at three years, and 48.4% at five years. In 2012, survival rates for CAPD patients in Thailand 79.2% at one year, 66% at three years, and 57% at five years. In 2006, CAPD patients in China had survival rates of 94% at one year, 81% at three years, and 64% at five years. Additionally, survival rates for CAPD patients in continental Europe in 2012 spanned 81.7% over a two-year period, and in Canada in 2013, one-year, two-year, and five-year survival rates were reported at 90%, 79%, and 50% respectively. Latin American CAPD patient survival rates in 2000 were observed at 91% at one year, 77% at three years, and 58% at five years. These outcomes suggest

relatively consistent 5-year CAPD survival rates exceeding 50% across both developing and developed countries (26-34).

The study also indicates that comorbidities and complications may contribute to increased mortality and reduced survival rates for CAPD patients. For instance, diabetes can cause hyperfiltration through efferent arteriolar vasoconstriction due to an active RAAS. CAPD patients with peritonitis may have a lower survival probability due to factors such as inadequate sanitary conditions, failure to strictly adhere to aseptic CAPD exchange protocols, severe malnutrition, and diabetes.

While the study provides valuable data on the prevalence and comorbidities of CAPD patients with UO, it is important to acknowledge its limitations. It was conducted on a small number of patients in a single centre. Therefore, it is suggested that future studies be carried out in multiple centres to obtain a more comprehensive understanding of the variables associated with the high survival rates of CAPD patients.

4. CONCLUSIONS

In the study's findings, the prevalence and concurrent conditions of CKD in patients undergoing CAPD and presenting with UO at Dr. Saiful Anwar General Hospital in Malang during 2023 were determined to be 6.50%. The data is predominantly comprised of males (57.8%) aged between 41 and 50 years (26%) with a high BMI (89.0%). Hypertension was identified as the highest risk factor (80.8%), and the obstruction was primarily unilateral (5.64%) with mild severity (4.06%).

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