CHAPTER II
LITERATURE REVIEW

A. Concept of Chronic Kidney Disease (CKD)

1. Definition

Chronic kidney disease (CKD) is a complex condition characterized by structural or functional impairment of the kidneys, resulting in the inability to maintain normal renal function. Consequently, excessive fluid and metabolic waste products accumulate in the bloodstream (Mailani *et al*., 2023).

CKD is defined as abnormalities of kidney structure or function that persist for more than three months and have implications for health. The disease is classified according to its underlying cause, glomerular filtration rate (GFR categories G1–G5), and degree of albuminuria (A1–A3), collectively referred to as the CGA classification (Cause, GFR category, and Albuminuria category) (Levey *et al*., 2020).

CKD is also characterized by kidney damage or a reduction in glomerular filtration rate (GFR) to less than 60 mL/min/1.73 m^2 for at least three months (Vaidya & Aeddula, 2025). In addition, the disease may be identified by the presence of albuminuria with an albumin-to-creatinine ratio of ≥30 mg/g (≥3 mg/mmol), abnormalities in urinary sediment or persistent hematuria, electrolyte disturbances, and other abnormalities resulting from tubular dysfunction (Stevens *et al*., 2024).

Based on the definitions presented above, chronic kidney disease (CKD) can be summarized as a progressive disorder characterized by structural or functional abnormalities of the kidneys that persist for more than three months. The condition is manifested by impaired renal filtration and/or clinical abnormalities such as albuminuria, persistent hematuria, electrolyte disturbances, or other markers of kidney damage.

CKD is classified according to its underlying cause, glomerular filtration rate (G1–G5), and degree of albuminuria (A1–A3). As the disease progresses, many patients eventually require kidney replacement therapy, including dialysis or kidney transplantation.

2. Etiology

Chronic kidney disease (CKD) may result from disease processes classified into three major categories, prerenal disorders (reduced renal perfusion pressure), intrinsic renal disorders (pathology involving the renal vasculature, glomeruli, or tubulointerstitium), and postrenal (obstructive) disorders (Vaidya & Aeddula, 2025). The etiologies of CKD according to Vaidya & Aeddula (2025), are described as follows:

a. Prerenal Disorders

Chronic prerenal disease commonly occurs in patients with chronic heart failure or liver cirrhosis, in whom persistent reduction in renal perfusion increases the risk of intrinsic kidney injury, particularly acute tubular necrosis (ATN). Over time, sustained renal hypoperfusion may lead to progressive deterioration of kidney function and ultimately contribute to the development of chronic kidney disease.

b. Intrinsic Renal Disorders

1) Intrinsic Renal Vascular Disease

The most common form of intrinsic renal vascular disease is nephrosclerosis, a condition characterized by progressive damage to the renal blood vessels, glomeruli, and tubulointerstitial tissues. Renal artery stenosis caused by atherosclerosis or fibromuscular dysplasia is also included in this category and may gradually progress to ischemic nephropathy over months to years. The principal pathological manifestations include glomerulosclerosis and tubulointerstitial injury.

2) Intrinsic Glomerular Disease

Intrinsic glomerular disease may present as either nephritic syndrome or nephrotic syndrome. The nephritic pattern is typically

characterized by abnormal urinary microscopic findings, including red blood cell casts, dysmorphic erythrocytes, and occasionally leukocytes, accompanied by varying degrees of proteinuria. Common causes include post-infectious glomerulonephritis, infective endocarditis, immunoglobulin A (IgA) nephropathy, lupus nephritis, Goodpasture syndrome, and systemic vasculitis.

3) Intrinsic Tubulointerstitial Disease

Among chronic tubulointerstitial disorders, polycystic kidney disease is one of the most frequently encountered conditions. Other etiologies include nephrocalcinosis, which is commonly associated with hypercalcemia and hypercalciuria, as well as sarcoidosis, Sjögren syndrome, and reflux nephropathy, all of which may occur in both pediatric and young adult populations.

c. Postrenal (Obstructive) Nephropathy

Chronic urinary tract obstruction may result from various conditions, including prostate disease, nephrolithiasis, and abdominal or pelvic tumors that exert compressive effects on the ureters. Congenital abnormalities involving the ureteropelvic junction or ureterovesical junction are also recognized causes of obstructive nephropathy. Less common etiologies include retroperitoneal fibrosis and neurogenic bladder, both of which may contribute to chronic obstruction and progressive impairment of renal function.

3. Risk Factors

The progression of chronic kidney disease (CKD) is influenced by multiple risk factors that can be classified into several major categories. Demographic factors, such as advanced age and sex, increase an individual's susceptibility to CKD. Genetic predisposition also contributes to the risk of impaired kidney function. In addition, cardiovascular conditions, particularly hypertension and heart disease, are major contributors that accelerate CKD progression. Metabolic factors, including diabetes mellitus, parathyroid hormone abnormalities, hemoglobin levels, serum uric acid, and

dyslipidemia, have also been associated with progressive deterioration of renal function. Furthermore, unhealthy lifestyle behaviors, such as excessive salt and fat intake, obesity, smoking, and physical inactivity, substantially increase the risk of developing CKD (Atkinson *et al*., 2021; Hannan *et al*., 2021; Maringhini & Zoccali, 2024).

According to the Indonesian Renal Registry (2020), hypertensive kidney disease is the leading cause of CKD in Indonesia, accounting for approximately 35% of all cases. Diabetic nephropathy is the second most common cause (29%), followed by primary glomerulopathy (8%). In addition, approximately 16% of CKD cases are classified as having an unknown etiology (Pernefri, 2020). The major causes of CKD are described as follows:

a. Hypertension

Hypertension is one of the leading risk factors for chronic kidney disease. Blood pressure is considered elevated when systolic blood pressure exceeds 120 mmHg or diastolic blood pressure exceeds 80 mmHg, whereas hypertension is generally defined as a blood pressure of ≥140/90 mmHg. Persistent uncontrolled hypertension damages the renal arteries, reduces blood flow to the nephrons, and subsequently causes renal ischemia and sclerosis, leading to progressive impairment of kidney function (Gultom & Sudaryo, 2023).

b. Diabetic Nephropathy

Diabetic nephropathy is the most common cause of chronic kidney damage and results from prolonged hyperglycemia. Chronic hyperglycemia progressively damages the glomerular capillaries, impairing the kidneys' filtration function and ultimately increasing the risk of progression to chronic kidney disease and kidney failure (Suherman *et al*., 2023).

c. Primary Glomerulopathy

Primary glomerulopathy refers to a group of kidney disorders that primarily affect the glomeruli, the microscopic filtering units

responsible for removing waste products from the blood. Damage to the glomeruli disrupts the normal filtration process, leading to structural and functional abnormalities that may manifest as progressive decline in renal function and other clinical complications associated with chronic kidney disease (Kyneissia Gliselda, 2021).

4. Pathophysiology

The concept of renal functional reserve plays a crucial role in understanding the progression of kidney disease, particularly chronic kidney disease (CKD). During the early stages of CKD, the glomerular filtration rate (GFR) may remain within the normal range; however, the renal functional reserve is often already diminished. This reduction reflects the presence of subclinical kidney damage that may not yet be detectable through conventional GFR assessment. As the disease progresses, the kidney gradually loses its ability to recruit additional nephrons to maintain renal function, eventually resulting in the complete depletion of renal functional reserve. A similar phenomenon is observed in acute kidney injury (AKI), where reduced renal functional reserve increases susceptibility to kidney injury because the kidneys no longer possess sufficient adaptive capacity to respond to additional physiological stress. Therefore, renal functional reserve is increasingly recognized as an important parameter for identifying individuals at high risk of developing CKD (Maringhini & Zoccali, 2024).

Chronic kidney disease is fundamentally characterized by progressive and irreversible renal fibrosis, resulting in permanent structural and functional impairment of the kidneys. The pathological process begins with persistent kidney injury, which triggers the infiltration of inflammatory cells into the renal tissue. This inflammatory response initiates a cascade of molecular and cellular events that promotes apoptosis and the loss of functional renal cells while simultaneously activating fibroblasts and myofibroblasts. Activated myofibroblasts produce excessive amounts of extracellular matrix proteins, leading to progressive fibrosis and the

replacement of normal renal parenchyma with fibrotic tissue. Consequently, renal architecture becomes increasingly distorted, resulting in a gradual decline in kidney function. This pathological process is further accelerated by uncontrolled hypertension and hyperglycemia, both of which perpetuate chronic inflammation, oxidative stress, and fibrotic signaling pathways, thereby contributing to the progression of CKD (Vaidya & Aeddula, 2025).

5. Classification

Chronic kidney disease (CKD) is classified using the CGA classification system, which is based on three components: Cause (C), glomerular filtration rate (GFR) category (G1–G5), and albuminuria category (A1–A3). These components play essential roles in assessing patients' clinical status, determining disease severity, and predicting the risk of disease progression. The CGA classification emphasizes that CKD should not be diagnosed solely on the basis of a reduced glomerular filtration rate (GFR) or an increased urine albumin-to-creatinine ratio (ACR) exceeding 30 mg/g (≥ 3 mg/mmol). Rather, the diagnosis may also be established by the presence of other markers of kidney damage. Nevertheless, in clinical practice, the CGA classification primarily focuses on two key dimensions GFR category and albuminuria category because both are strongly associated with disease progression and clinical outcomes. A clear understanding of this classification is essential, as these important distinctions are often overlooked by healthcare professionals and students alike. Failure to recognize these concepts may compromise diagnostic accuracy, risk stratification, and the comprehensive management of patients with CKD (Stevens *et al*., 2024).

Table 2.1 Classification of Chronic Kidney Disease

Chronic Kidney Disease (CKD) is classified according to the Cause (C), Glomerular Filtration Rate (GFR; G), and Albuminuria (A) (CGA Classification).			Persistent Albuminuria Categories and Description		
			A1	A2	A3
			Normal to mildly increased	Moderately increased	Severely increased
			< 30 mg/g < 3 mg/mmol	30–300 mg/g 3–30 mg/mmol	> 300 mg/g > 30 mg/mmol
GFR Category (mL/min/1.73 m²) Description and Range					
G1	Normal or high	≥ 90			
G2	Mildly decreased	60–89			
G3a	Mildly to moderately decreased	45–59			
G3b	Moderately to severely decreased	30–44			
G4	Severely decreased	15–29			
G5	Kidney failure	< 15			

Low risk *(if no other markers of kidney damage are present, CKD is not diagnosed).*
Moderately increased risk
High risk
Very high risk

Sources: (Stevens *et al*., 2024)

Table 2.2 Criteria for Chronic Kidney Disease

Markers of Kidney Damage (One or More)	Albuminuria (ACR ≥ 30 mg/g [≥ 3 mg/mmol]) Urinary sediment abnormalities Persistent hematuria Electrolyte abnormalities and other disorders resulting from tubular dysfunction Histological abnormalities Structural abnormalities detected by imaging History of kidney transplantation
Decreased GFR	GFR < 60 mL/min/1.73 m² (GFR categories G3a–G5)

Sources: (Stevens *et al*., 2024)

6. Clinical Manifestations

In the early stages, chronic kidney disease (CKD) is generally asymptomatic and therefore often remains undiagnosed. Clinical manifestations usually become apparent only when patients progress to advanced stages of the disease, particularly stages 4 and 5 (Vaidya & Aeddula, 2025). The common clinical manifestations include the following:

a. Nausea and vomiting

Nausea and vomiting are common manifestations of uremia and are primarily associated with the accumulation of nitrogenous waste products (e.g., urea, creatinine, and other metabolic by-products), acid–base imbalance, and delayed gastric emptying (Vaidya & Aeddula, 2025).

b. Loss of appetite

Loss of appetite in patients with CKD is multifactorial and may result from altered or metallic taste perception, chronic nausea, systemic inflammation, and depression (Vaidya & Aeddula, 2025).

c. Fatigue and weakness

Fatigue and weakness in patients with CKD have a multifactorial etiology, including chronic anemia, metabolic disturbances (e.g., amino acid abnormalities and metabolic acidosis), chronic inflammation, sleep disorders, and psychosocial factors (Gregg *et al*., 2021).

d. Sleep disturbances

Sleep disturbances in CKD are associated with uremia, altered melatonin secretion, anemia, pruritus, and cardiometabolic comorbidities. Early identification and appropriate management of sleep disorders, including sleep hygiene interventions and treatment for Restless Legs Syndrome (RLS) and Obstructive Sleep Apnea (OSA), may improve patients' daily functioning and overall quality of life (Tan *et al*., 2022).

e. Oliguria

Oliguria increases the risk of fluid and toxin accumulation. Therefore, careful monitoring of urine output, daily body weight, and appropriate adjustments to fluid management and pharmacological therapy are essential components of clinical care (Vaidya & Aeddula, 2025).

f. Cognitive impairment

Cognitive impairment in patients with CKD may result from the accumulation of uremic toxins, anemia, vascular dysfunction, and systemic inflammation (Kelly & Rothwell, 2022).

g. Muscle cramps

Muscle cramps are thought to result from electrolyte imbalances, particularly abnormalities in sodium, potassium, calcium, and magnesium levels, as well as metabolic acidosis and neuromuscular alterations associated with uremia (Stevens *et al*., 2024).

h. Swelling of the feet and ankles

Peripheral edema in CKD results primarily from sodium and water retention due to impaired renal function and may also be exacerbated by hypoalbuminemia. Significant peripheral edema is indicative of fluid overload and may progress to pulmonary edema if left untreated (Stevens *et al*., 2024).

i. Persistent pruritus

CKD-associated pruritus is a chronic symptom that is frequently underestimated despite its substantial impact on patients' quality of life, including sleep disturbances and depression. Its pathogenesis is multifactorial and involves the accumulation of uremic toxins, immune dysregulation, peripheral neuropathy, and abnormalities in phosphate and calcium metabolism (Thompson *et al*., 2024).

j. Chest pain due to uremic pericarditis

Uremic pericarditis is an inflammatory complication that occurs in patients with advanced kidney failure, particularly before or around the

initiation of kidney replacement therapy. It may present with chest pain and a pericardial friction rub and can progress to life-threatening cardiac tamponade if not promptly recognized and treated (Rhabneh & Rout, 2025).

k. Dyspnea due to pulmonary edema caused by fluid overload

Systemic fluid accumulation and elevated pulmonary circulatory pressure resulting from volume overload may lead to pulmonary edema and dyspnea (Stevens *et al*., 2024).

l. Hypertension

Hypertension in patients with CKD develops primarily as a consequence of sodium and fluid retention, activation of the renin–angiotensin–aldosterone system (RAAS), and vascular remodeling associated with declining kidney function (Stevens *et al*., 2024).

Meanwhile, according to Vaidya & Aeddula (2025), physical examination findings are often insufficient for the early detection of chronic kidney disease (CKD). However, patients may present with the following clinical manifestations:

a. Skin hyperpigmentation

Patients frequently develop diffuse hyperpigmentation due to the accumulation of uremic toxins and impaired melanin metabolism. This manifestation is more commonly observed in advanced stages of CKD and is often accompanied by dry or scaly skin (Goel *et al*., 2021).

b. Excoriations secondary to pruritus

Chronic kidney disease-associated pruritus (CKD-aP) is one of the most distressing symptoms affecting patients' quality of life. Its pathophysiology is associated with the accumulation of uremic toxins, chronic inflammation, and disturbances in mineral metabolism. Clinically, patients often exhibit excoriations or scratch marks, particularly on the back and extremities (Bai *et al*., 2025).

c. Pericardial friction rub due to uremic pericarditis

Pericardial inflammation resulting from severe azotemia is characterized by chest pain and the presence of a pericardial friction rub on auscultation. This condition represents a serious complication of CKD and requires prompt initiation of kidney replacement therapy (Rhabneh & Rout, 2025).

d. Uremic frost

Markedly elevated blood urea nitrogen (BUN) levels may cause urea excreted through sweat to crystallize on the skin surface, forming a fine white powder known as uremic frost (Almustanyir & Abu-Zaid, 2020).

e. Hyperreflexia and muscle twitching

Hyperreflexia, muscle twitching, and muscle cramps commonly occur as a result of electrolyte imbalances and the accumulation of uremic toxins. If left untreated, these neurological manifestations may progress to uremic encephalopathy (Rout *et al*., 2025).

f. Hypertensive funduscopic changes indicating chronic disease

Long-standing hypertension may lead to hypertensive retinopathy, characterized by arteriolar narrowing, retinal hemorrhages, and hard exudates. These funduscopic findings indicate chronic hypertension and reflect its contribution to the progression of chronic kidney disease (Tripathy *et al*., 2025).

7. Complications

Chronic kidney disease (CKD) not only impairs the kidneys' excretory function but also leads to various systemic complications associated with disturbances in fluid balance, metabolism, hematologic function, and the cardiovascular system. These complications become increasingly pronounced as the disease progresses, particularly in stages 4 and 5, thereby requiring close monitoring and comprehensive, integrated management (Vaidya & Aeddula, 2025).

According to Vaidya & Aeddula (2025), the common complications experienced by patients with CKD include the following:

a. Fluid and electrolyte imbalance, sodium and water retention may increase blood pressure, although this condition is not always accompanied by edema.
b. Hypertension, hypertension is one of the most common complications of CKD and is a major contributor to cardiovascular risk. Current clinical guidelines recommend maintaining systolic blood pressure at approximately 120–130 mmHg and diastolic blood pressure at 70–80 mmHg, accompanied by regular monitoring to optimize treatment outcomes.
c. Hyperkalemia, patients with CKD are particularly susceptible to hyperkalemia, especially in the presence of oliguria, impaired distal tubular function, or the use of medications such as angiotensin-converting enzyme (ACE) inhibitors and nonselective beta-blockers, which may further increase the risk of hyperkalemia.
d. Metabolic acidosis, metabolic acidosis is another common complication resulting from the accumulation of acidic metabolic products due to impaired renal acid excretion.
e. Hyperphosphatemia, hyperphosphatemia commonly occurs in CKD as a consequence of reduced renal phosphate filtration and excretion.
f. Anemia, from a hematological perspective, anemia is an almost universal complication among patients with advanced CKD, primarily due to inadequate erythropoietin production by the diseased kidneys.
g. Cardiovascular disease, the risk of cardiovascular disease increases progressively with advancing CKD and remains the leading cause of morbidity and mortality in this population.
h. Insulin resistance, insulin resistance is also frequently observed in patients with CKD. This condition is closely associated with metabolic syndrome and atherosclerosis and is largely mediated by increased levels of inflammatory mediators.

8. Pharmacological Management

The general pharmacological management of patients with chronic kidney disease (CKD) emphasizes the importance of adjusting medication dosages according to the estimated glomerular filtration rate (*eGFR*) to prevent drug toxicity and therapeutic failure (Vaidya & Aeddula, 2025).

For adult patients with CKD stages 1–5 or those who have undergone kidney transplantation, the Kidney Disease Outcomes Quality Initiative (KDOQI) recommends vitamin D supplementation (*cholecalciferol* or *ergocalciferol*) to correct deficiency or insufficiency of 25-hydroxyvitamin D (25[OH]D). In patients with nephrotic-range proteinuria, supplementation with *cholecalciferol*, *ergocalciferol*, or other safe and effective 25(OH)D precursors may also be considered. Meanwhile, for patients with CKD undergoing dialysis, the kidney disease Improving Global Outcomes (KDIGO) guidelines recommend against initiating statin therapy or statin/*ezetimibe* combination therapy. In addition, nephrotoxic agents, including aminoglycosides, *nonsteroidal anti-inflammatory drugs* (NSAIDs), and radiographic contrast media, should be avoided whenever possible (Ministry of Health, 2023).

9. Non-Pharmacological Management

In addition, preparation for kidney replacement therapy should be carefully planned. This includes referral for surgical creation of vascular access for hemodialysis or placement of a peritoneal dialysis catheter, as well as evaluation of eligibility for kidney transplantation when clinically indicated (Vaidya & Aeddula, 2025).

According to Vaidya & Aeddula (2025), , once patients progress to Stage 4 chronic kidney disease (CKD), they should be provided with comprehensive information regarding the available kidney replacement therapy options. These options include the following:

a. Hemodialysis and peritoneal dialysis, which may be performed either continuously or intermittently in specialized healthcare facilities,

depending on the patient's clinical condition and treatment requirements.

b. Kidney transplantation, using either a living or deceased donor, is considered the preferred treatment option for eligible patients with CKD because it has been shown to provide superior long-term clinical outcomes.

c. For patients who decline kidney replacement therapy, healthcare professionals should provide education regarding conservative kidney management and palliative care as alternative treatment approaches aimed at optimizing quality of life and symptom control.

d. Hemodialysis can only be initiated after a stable vascular access has been established. Vascular access is typically created in the non-dominant upper extremity to minimize interference with the patient's daily activities.

B. Concept of Hemodialysis

1. Definition

Hemodialysis is a kidney replacement therapy designed to remove metabolic waste products and excess fluid from the body while maintaining physiological homeostasis. It is the most widely used form of kidney replacement therapy for patients with end-stage kidney disease (Utami *et al*., 2023). Hemodialysis is an extracorporeal blood purification process in which blood is diverted from the body to a dialysis machine that removes metabolic waste products and excess fluid. The procedure requires the establishment of vascular access by creating an arteriovenous fistula (AVF) or placing a vascular graft, both of which serve as access points to the dialyzer. Once the vascular access is functional, maintenance hemodialysis is typically performed three times per week, with each session lasting approximately 4–5 hours. After the blood has been filtered through the dialyzer, it is returned to the patient's circulation through the same vascular (Australian Institute of Health and Welfare, 2023).

Hemodialysis is initiated after a stable vascular access has been established, preferably in the nondominant arm. The use of peripheral intravenous cannulas in this arm should be avoided to preserve venous integrity for future vascular access. The preferred vascular access is an arteriovenous fistula (AVF). Alternative forms of vascular access include an arteriovenous graft (AVG) and a tunneled hemodialysis catheter, commonly referred to as a catheter double lumen (CDL). An arteriovenous fistula is considered the optimal vascular access because of its superior long-term patency, lower risk of infection, higher achievable blood flow rates, and reduced risk of recirculation compared with other vascular access modalities (Vaidya & Aeddula, 2025).

Based on the literature reviewed, hemodialysis can be defined as a kidney replacement therapy that removes metabolic waste products and excess fluid by circulating blood through an extracorporeal dialyzer before returning the purified blood to the body via vascular access. Maintenance hemodialysis is generally performed three times per week, with each treatment session lasting approximately 4–5 hours.

2. Principles and Mechanism of Hemodialysis

At the beginning of a hemodialysis session, a dialysis nurse or technician inserts two needles into the patient's vascular access, typically in the arm. Each needle is connected to flexible tubing attached to the hemodialysis machine. During the procedure, the patient's blood passes through a filter known as a dialyzer, often referred to as an artificial kidney because it performs many of the filtration functions of the native kidneys outside the body. The dialyzer removes metabolic waste products, excess electrolytes, and excess fluid from the blood before returning the purified blood to the patient's circulation. The hemodialysis machine pumps blood into one end of the dialyzer, where it flows through thousands of fine hollow fibers. Simultaneously, the dialysate solution flows in the opposite direction along the outside of these hollow fibers. This countercurrent flow facilitates the diffusion of waste products and excess electrolytes from the blood into

the dialysate, while ultrafiltration removes excess fluid. The purified blood remains within the hollow fibers and is subsequently returned to the patient's body. Throughout the hemodialysis session, the dialysis machine continuously monitors blood pressure and regulates both the blood flow rate through the dialyzer and the rate of fluid removal to ensure the safety and effectiveness of the treatment (National Institute of Diabetes and Digestive and Kidney Diseases, 2025).

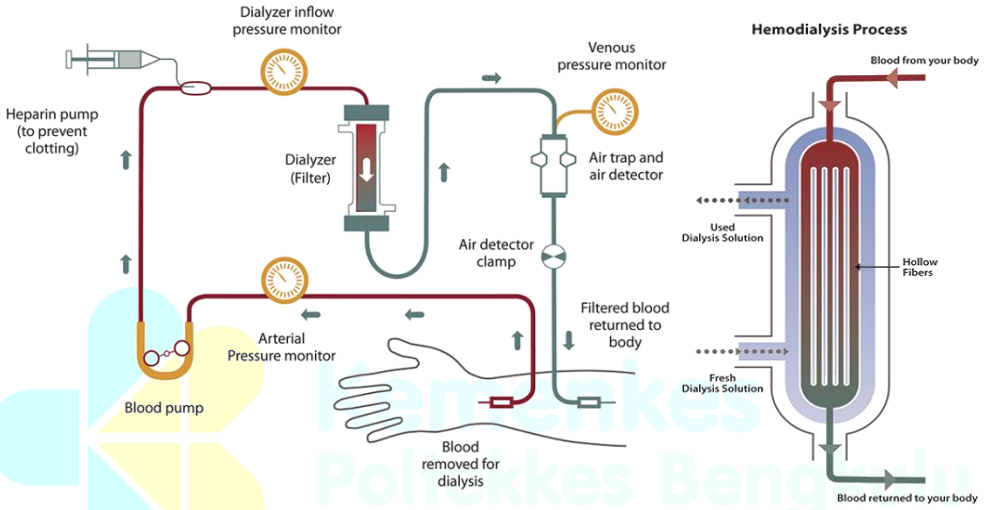

Figure 2.1 Principles and Mechanisms of Hemodialysis

Sources: (National Institute of Diabetes and Digestive and Kidney Diseases, 2025).

3. Objectives of Hemodialysis

According to the National Kidney Foundation (2023), dialysis partially replaces kidney function by helping maintain the body's physiological balance (National Kidney Foundation, 2023). The primary objectives of hemodialysis include the following National Kidney Foundation (2023), such as:

a. To remove metabolic waste products and excess body fluids, thereby preventing their accumulation in the body.
b. To maintain the balance of essential blood electrolytes, including potassium, sodium, calcium, and bicarbonate.
c. To help regulate blood pressure and maintain it within the normal range.

4. Benefits of Hemodialysis

Hemodialysis is a highly effective treatment for removing metabolic waste products and excess fluid from the blood. However, it does not completely replace all kidney functions and, therefore, is not considered a cure for advanced chronic kidney disease or kidney failure. In cases of acute kidney injury (AKI), hemodialysis may be required only temporarily until kidney function recovers. However, when chronic kidney disease progressively advances to kidney failure, kidney function is generally irreversible. Consequently, patients require lifelong dialysis unless they undergo a successful kidney transplantation (National Kidney Foundation, 2023).

5. Indications and Contraindications for Hemodialysis

a. Indications for Hemodialysis

The initiation of hemodialysis is indicated in acute clinical conditions. These conditions result in immune system dysregulation and impaired cytokine clearance, with cytokines acting as key mediators of the immune response. Consequently, they may trigger vasodilation, reduced cardiac function, and immunosuppression, ultimately leading to target organ damage, hemodynamic instability, and delayed recovery of kidney function (Murdeshwar & Anjum, 2025).

According to Murdeshwar & Anjum (2025), the indications for hemodialysis include the following:

1) Acute kidney injury.
2) Uremic encephalopathy.
3) Pericarditis.
4) Life-threatening hyperkalemia.
5) Refractory metabolic acidosis.
6) Hypervolemia resulting in end-organ complications (e.g., pulmonary edema).
7) Growth failure and malnutrition.
8) Peripheral neuropathy.

9) Refractory gastrointestinal symptoms.
10) Asymptomatic patients with an estimated glomerular filtration rate (eGFR) of 5–9 mL/min/1.73 m².
11) Intoxication with any dialyzable toxin.

b. Contraindications for Hemodialysis

The only absolute contraindication to hemodialysis is the inability to establish vascular access. Relative contraindications include difficult vascular access, needle phobia, severe heart failure, and coagulation disorders that impair normal blood clotting. Advances in medical technology have enabled the successful creation and maintenance of vascular access even in patients with extensive vascular disease. Needle phobia can often be managed with local anesthesia and appropriate nursing support. When a patient refuses dialysis, this decision should be respected; however, the nephrologist should ensure that no potentially reversible factors, such as severe anxiety or depression that may impair the patient's decision-making capacity, are present. In such cases, psychiatric evaluation may be warranted. For patients with severe comorbidities, conservative management may be considered as an alternative while optimizing all appropriate non-dialytic therapies. If an acceptable quality of life cannot be maintained, hemodialysis should be avoided because the potential survival benefit may not outweigh the associated treatment burden and discomfort (Murdeshwar & Anjum, 2025).

6. Complications and Side Effects of Hemodialysis

a. Hemodialysis Complications

Several complications associated with hemodialysis constitute medical emergencies that require the immediate discontinuation of dialysis, clamping of the blood lines, and supportive management before definitive treatment, such as kidney transplantation. One of the most serious complications is Dialysis Disequilibrium Syndrome (DDS), which occurs more frequently during the initial hemodialysis

session. This condition is characterized by neurological deterioration, including restlessness, confusion, headache, seizures, and even coma, resulting from a urea concentration gradient between the blood and cerebrospinal fluid that leads to cerebral edema (Murdeshwar & Anjum, 2025).

According to Murdeshwar & Anjum (2025), the most common complications associated with hemodialysis include the following:

1) Intradialytic hypotension is one of the most common complications and is associated with an increased risk of mortality and cardiac dysfunction, including myocardial stunning. A systolic blood pressure below 90 mmHg is strongly associated with an increased risk of death. Clinical manifestations include dizziness, lightheadedness, nausea, and other mild symptoms.
2) Muscle cramps frequently occur as a consequence of hypotension, a high ultrafiltration rate, hypovolemia, or the use of low-sodium dialysate. These factors induce vasoconstriction and reduce muscle perfusion, thereby impairing muscle relaxation.
3) Air embolism is a potentially fatal complication characterized by the presence of air bubbles in the venous dialysis circuit and a characteristic churning or splashing sound detected during chest auscultation.
4) Other nonspecific complications include nausea, vomiting, headache, chest pain, back pain, and pruritus.
5) Vascular access dysfunction, most commonly resulting from arteriovenous stenosis, is a major contributor to reduced quality of life among patients undergoing hemodialysis.
6) Hemodialysis may also cause electrolyte disturbances, including hyperkalemia, hypermagnesemia, hyponatremia, and hypocalcemia.

b. Side Effects of Hemodialysis

Each individual responds differently to hemodialysis, and the risk of experiencing complications or side effects varies among patients. Moreover, it is often difficult to determine whether certain symptoms are attributable to the dialysis procedure itself or to kidney failure, which also affects multiple body systems (National Kidney Foundation, 2023).

According to the National Kidney Foundation, (2023), the most commonly reported side effects of hemodialysis include the following:

1) Blockage of the vascular access site.
2) Muscle cramps.
3) Hypotension (low blood pressure).
4) Weakness, dizziness, or nausea.
5) Blood loss.
6) Excessive weight gain.
7) Skin and bloodstream infections, which, if left untreated, may progress to sepsis, a life-threatening condition characterized by multiple organ dysfunction.
8) Fatigue, this condition may affect any patient receiving hemodialysis but is more commonly observed among individuals who have undergone dialysis for an extended period. It is often difficult to determine whether fatigue is a side effect of dialysis or a symptom of chronic kidney disease itself.
9) Pruritus, or persistent itching of the skin, is commonly experienced by patients with chronic kidney disease, particularly those with advanced-stage disease and those undergoing dialysis. Similar to fatigue, it is often difficult to determine whether pruritus represents a side effect of dialysis or a manifestation of chronic kidney disease.

C. Concept of Fatigue in Patients Undergoing Hemodialysis

1. Definition and Characteristics of *Fatigue* in Patients Undergoing Hemodialysis

Fatigue in patients undergoing maintenance hemodialysis (HD) is not merely a sensation of ordinary tiredness; rather, it is a complex, multidimensional phenomenon encompassing physical, psychological, and emotional components. It may persist chronically throughout the day and is closely associated with the dialysis cycle, including *intradialytic fatigue* (IDF), which develops or worsens during the dialysis session, and *post-dialysis fatigue* (PDF), which occurs or intensifies after treatment and may persist for several hours (Bossola *et al*., 2023).

This condition is defined as a persistent and debilitating sense of tiredness and weakness that substantially impairs patients' ability to perform daily activities and diminishes their quality of life. The principal characteristics of fatigue include sustained energy depletion, impaired cognitive function, and difficulty maintaining concentration (Alshammari *et al*., 2024; Mailani *et al*., 2025).

Clinically, patients describe fatigue as feelings of weakness, low energy, being worn out, exhausted, or experiencing an urge to collapse following a hemodialysis session. They frequently report a sensation of bodily heaviness, slowed physical movement, difficulty concentrating or thinking clearly, reduced tolerance for even light physical activities, and feelings of emotional exhaustion or hopelessness (Al-Naamani *et al*., 2025; Bossola *et al*., 2023; Mailani *et al*., 2025).

2. Pathophysiology of Fatigue in Patients Undergoing Hemodialysis

Patients with chronic kidney disease (CKD) develop lactic acidosis more rapidly than healthy individuals in response to low levels of physical activity, which may contribute to muscle fatigue. Patient-reported fatigue has been shown to correlate with higher plasma lactate concentrations and an increased respiratory exchange ratio in individuals with CKD, suggesting that enhanced anaerobic metabolism plays an important role in the

pathophysiology of fatigue. In addition, the combination of anemia and impaired cardiovascular compensatory mechanisms reduces oxygen delivery to peripheral tissues, contributing to lactic acidosis and fatigue. These conditions decrease arterial oxygen-carrying capacity and impair systemic oxygen transport, thereby exacerbating fatigue symptoms. Consequently, anemia has consistently been identified as one of the most common risk factors associated with fatigue in patients with CKD (Gregg *et al*., 2021).

Another major contributor to fatigue is the accumulation of metabolic waste products, commonly referred to as uremic toxins, in the bloodstream as a result of impaired kidney function. These toxins exert detrimental cellular effects by disrupting mitochondrial function, impairing energy metabolism, and reducing skeletal muscle performance. As a result, patients experience diminished physical endurance and persistent fatigue, which substantially compromises their functional capacity and overall quality of life (Alshammari *et al*., 2024).

3. Signs and Symptoms of Fatigue in Patients Undergoing Hemodialysis

Subjective symptoms, including tiredness, weakness, and loss of energy, are among the most common complaints reported by patients with chronic kidney disease (CKD) undergoing maintenance hemodialysis (Santoso *et al*., 2022).

Other common physical manifestations include an increased need for daytime sleep, and in severe cases, patients may feel too exhausted even to eat. The long-term consequences of these functional limitations often include an inability to work or maintain employment, which can subsequently have detrimental effects on financial stability, self-confidence, and overall quality of life (Alshammari *et al*., 2024).

From a cognitive perspective, patients frequently report impaired cognitive function and difficulty concentrating. Emotionally, the impact of fatigue can be substantial. Patients often express frustration at being too exhausted to engage in activities they wish to perform. Furthermore, some

individuals may become irritable without an apparent reason and experience unpredictable mood fluctuations as a consequence of persistent fatigue (Al-Naamani *et al*., 2025; Mailani *et al*., 2025).

4. Factors Influencing Fatigue in Patients Undergoing Hemodialysis

The accumulation of metabolic waste products, fluid and electrolyte imbalances, abnormal energy expenditure, anemia, and depression are recognized contributors to fatigue among patients undergoing hemodialysis (Khoirunnisa *et al*., 2024).

A wide range of physical and psychosocial factors, including age, educational level, employment status, comorbidities, duration of hemodialysis, changes in systolic blood pressure, hemoglobin (Hb) level, interdialytic weight gain (IDWG), and health literacy, have also been reported to be significantly associated with fatigue severity (Mailani *et al*., 2025). Overall, fatigue in patients undergoing hemodialysis results from the complex interaction of multiple contributing factors. Therefore, effective management strategies should adopt a multidisciplinary approach that addresses medical, psychological, and social aspects of patient care (Xia *et al*., 2025).

Based on the study conducted by Xia *et al*. (2025), fatigue in patients undergoing hemodialysis is influenced by multidimensional factors, including the following:

a. Sociodemographic factors

Older age, female sex, lower educational attainment, unemployment, and limited social support have been shown to be associated with greater fatigue severity. In contrast, patients who are employed or receive stronger social support tend to report lower levels of fatigue, likely because of positive distraction and more effective coping mechanisms.

b. Physiological factors

Anemia, malnutrition or protein-energy wasting (PEW), and systemic inflammation, as indicated by elevated C-reactive protein

(CRP) and interleukin-6 (IL-6) levels, contribute to fatigue. Furthermore, comorbid conditions such as diabetes mellitus, cardiovascular disease, and chronic obstructive pulmonary disease (COPD) have been associated with increased fatigue severity. Uremic symptoms, including restless legs syndrome (RLS) and pruritus, may further exacerbate fatigue in patients undergoing hemodialysis.

c. Psychological factors

Depression, anxiety, and sleep disorders, including insomnia and sleep apnea, are strongly associated with fatigue. These conditions often create a vicious cycle in which fatigue aggravates psychological symptoms, while psychological distress, in turn, intensifies fatigue.

d. Treatment-related factors

Hemodialysis itself may induce post-dialysis fatigue, particularly as a result of intradialytic hypotension, rapid ultrafiltration, or inadequate dialysis. In addition, medications such as beta-blockers, antidepressants, and sleep medications have been reported to be associated with fatigue, either because of their adverse effects or the underlying conditions for which they are prescribed.

Another factor that may contribute to fatigue in patients undergoing hemodialysis is the type of vascular access used. In patients with an immature or stenotic arteriovenous fistula (AVF), reduced blood flow may compromise dialysis adequacy, thereby contributing to fatigue. Conversely, the use of a catheter double lumen (CDL), which is associated with a higher risk of infection, thrombosis, and other complications, may increase both physical and psychological burden, ultimately exacerbating fatigue (Nenova & Yankov, 2025; Venegas-Ramírez *et al*., 2025).

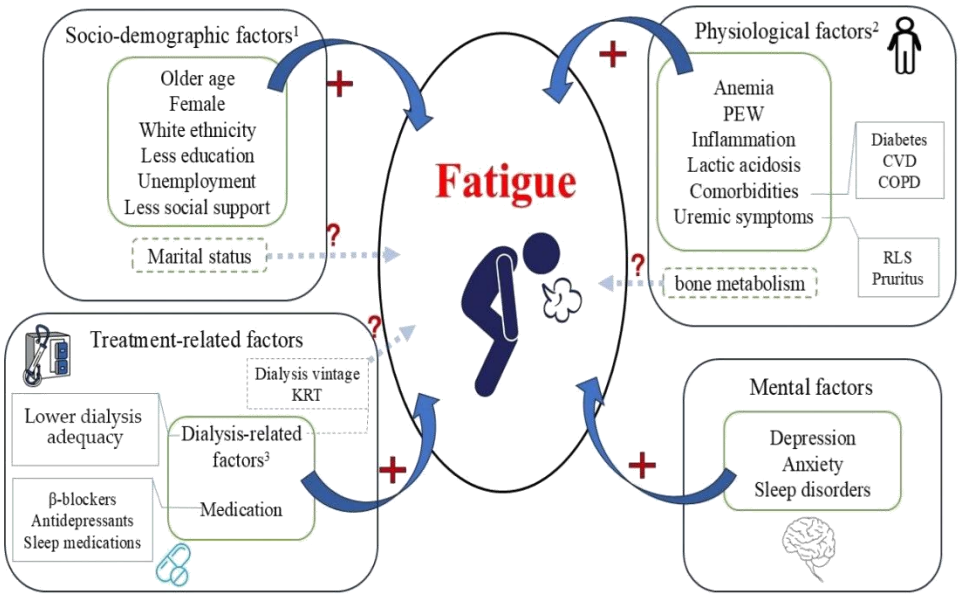

Figure 2.2 Factors Influencing Fatigue in Patients Undergoing Hemodialysis

Sources: (Xia *et al*., 2025)

5. Fatigue Assessment Instrument for Patients Undergoing Hemodialysis

Currently, there is no universal consensus regarding the most appropriate instrument for assessing fatigue in patients with chronic kidney disease (CKD). Most available questionnaires use a Likert scale to generate fatigue scores. Some instruments assess multiple dimensions of fatigue, whereas others rely on a single global question to evaluate the presence and severity of fatigue or the individual's overall energy level. Among the instruments that have been evaluated in patients with CKD, the *Functional Assessment of Chronic Illness Therapy–Fatigue* (FACIT-Fatigue) Scale is the only multidimensional questionnaire specifically developed to comprehensively assess various aspects of fatigue. Version 4 of the *FACIT-Fatigue* Scale is part of the *Health-Related Quality of Life* (HRQOL) measurement system, which was developed to evaluate the impact of chronic diseases on patients' functional well-being and quality of life (Gregg *et al*., 2021; Mailani *et al*., 2025).

The Indonesian version of the FACIT-Fatigue Scale Version 4 is a concise questionnaire consisting of 13 items. It includes questions

specifically designed to assess fatigue severity and has been shown to be practical, easy to administer, and easily understood by patients with chronic kidney disease undergoing maintenance hemodialysis. Consequently, this questionnaire is recommended for evaluating the level of fatigue experienced during routine daily activities over the previous seven days. Responses are rated on a five-point Likert scale, with scores ranging from 4 (*not at all*), 3 (*a little bit*), 2 (*somewhat*), 1 (*quite a bit*), to 0 (*very much*). However, for Items 7 and 8, the scoring is reversed, with 0 corresponding to *not at all* and 4 corresponding to *very much* (Sihombing *et al*., 2016; Tennant, 2019).

The *Functional Assessment of Chronic Illness Therapy* (FACIT) Scale has demonstrated satisfactory validity and reliability. Validation of the Indonesian version of the FACIT-Fatigue Scale indicated that all questionnaire items were valid, with correlation coefficients exceeding the critical value (r = 0.279). Reliability testing using Cronbach's alpha demonstrated acceptable internal consistency (Cronbach's α = 0.646), indicating that the instrument is reliable. The total score ranges from 0 to 52, with a maximum possible score of 52. Scores below 30 indicate severe fatigue, whereas higher scores reflect lower fatigue severity and better health-related quality of life. Fatigue severity is classified as severe (scores of 0–29) and mild (scores of 30–52). Overall, the Indonesian version of the FACIT-Fatigue Scale Version 4 has been confirmed to be a valid and reliable instrument for measuring fatigue among patients with chronic kidney disease undergoing maintenance hemodialysis in Indonesia (Maesaroh & Agung, 2020; Sihombing *et al*., 2016; Tennant, 2019).

D. Concept of Vascular Access for Hemodialysis

1. Definition of Vascular Access

Vascular access is a vital pathway that supports the survival of patients with End-Stage Renal Disease (ESRD) or chronic kidney disease (CKD) who require maintenance hemodialysis. It provides a reliable route for

circulating blood from the patient's body to the hemodialysis machine and back while also allowing the direct administration of medications into the bloodstream. During the hemodialysis procedure, blood is transported through tubing to the dialysis machine, where it is filtered by a specialized membrane known as a dialyzer before being returned to the patient's circulation. An ideal vascular access should be reliable, durable, free from complications, and capable of delivering adequate dialysis according to the patient's clinical needs (Khosim & Dewi, 2025).

Vascular access is widely recognized as the *lifeline* of patients undergoing hemodialysis because the quality and continuity of dialysis treatment depend largely on its functionality. This surgically created access connects the patient's circulatory system to the hemodialysis machine, thereby facilitating the removal of metabolic waste products, excess fluid, and electrolyte imbalances during treatment (Lok *et al*., 2025). Consequently, vascular access serves not only as a technical requirement for hemodialysis but also as a critical determinant of patient morbidity, mortality, and health-related quality of life (Nousis *et al*., 2025).

2. Types of Vascular Access

In general, there are three main types of permanent vascular access for hemodialysis: arteriovenous fistula (AVF), arteriovenous graft (AVG), and central venous catheter (CVC) (Arasu *et al*., 2022). Among these, the vascular access methods most commonly used for hemodialysis are the arteriovenous fistula (AVF) and the catheter double lumen (CDL) (Muhtadini & Permana, 2024). The characteristics of each vascular access type commonly used in patients undergoing hemodialysis are described below:

a. Arteriovenous Fistula (AVF) Vascular Access

An arteriovenous fistula (AVF) is considered the preferred vascular access for maintenance hemodialysis because of its superior long-term durability and the lowest risk of complications, including thrombosis and infection. An AVF is surgically created by forming an anastomosis

between an artery and a vein, allowing high-pressure arterial blood to flow directly into the low-pressure venous system. This physiological change induces progressive venous dilation and thickening of the vessel wall, a process known as arterialization. Arterialization subsequently leads to fistula maturation, indicating that the AVF is suitable for cannulation and effective hemodialysis treatment. On average, an AVF requires approximately six weeks to mature; however, nearly 25% of fistulas fail to reach adequate maturation. Because the progression of kidney function decline is often difficult to predict, AVF creation is recommended approximately three to six months before hemodialysis is anticipated to be required (Arasu *et al*., 2022).

An arteriovenous fistula (AVF) provides a sufficiently large vascular diameter to support the high blood flow rates required for efficient hemodialysis, allowing blood to circulate rapidly from the patient to the dialysis machine and back to the body (National Institute of Diabetes and Digestive and Kidney Diseases, 2025).

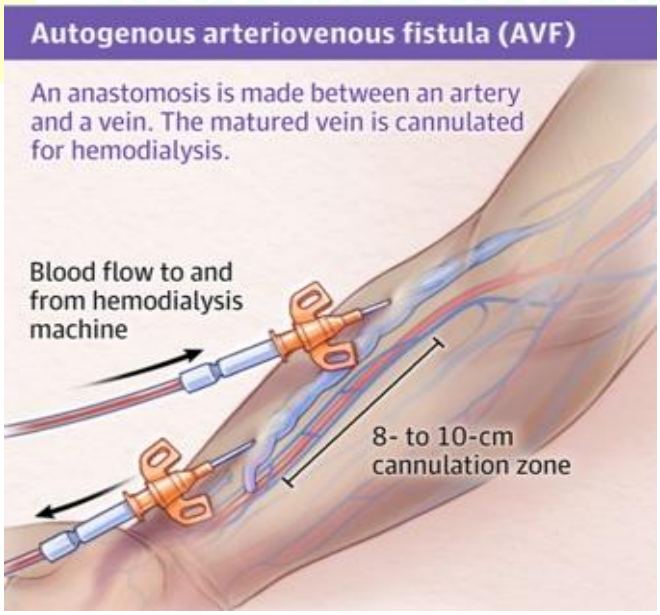

Figure 2.3 Arteriovenous Fistula (AVF) Vascular Access

Sources: (Lok *et al*., 2025)

b. Arteriovenous Graf (AVG) Vascular Access

An arteriovenous graft (AVG) is created by surgically implanting an expanded polytetrafluoroethylene graft within a subcutaneous tunnel, connecting the *inflow artery* to the *outflow vein* through surgical anastomoses. The graft is typically allowed to mature for at least two weeks before cannulation to facilitate adequate incorporation into the surrounding tissue. AVG configurations are generally classified into two types: the *forearm loop graft* and the *upper-arm straight graft*. The *forearm loop graft* is constructed in the forearm by connecting the brachial artery to the median cubital vein or cephalic vein. The graft is configured in a loop to provide a longer cannulation segment and facilitate repeated needle insertion. In contrast, the *upper-arm straight graft* is created in the upper arm by connecting the brachial artery to the axillary vein. The graft follows a straight or gently curved course and is typically used when vascular access in the forearm is not feasible (Arasu *et al*., 2022).

An AVG is generally considered when the patient's native blood vessels are unsuitable for arteriovenous fistula (AVF) creation. However, compared with AVF, AVG is associated with a higher risk of vascular complications, particularly stenosis and thrombosis (Hassanein *et al*., 2025).

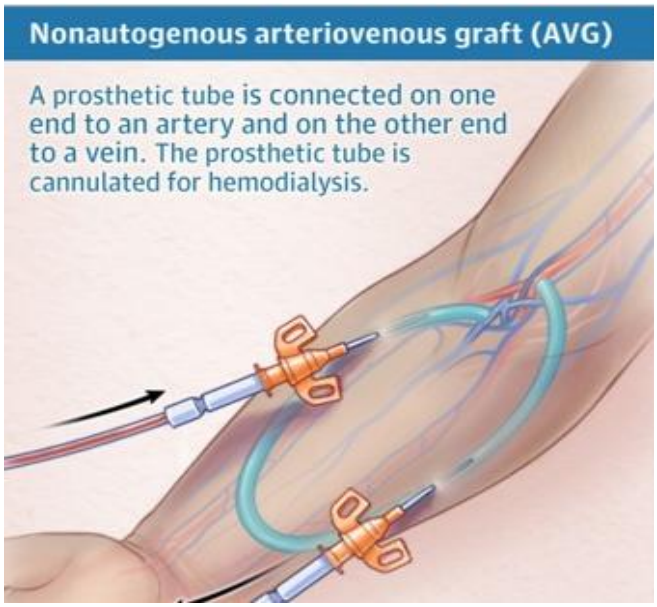

Figure 2.4 Arteriovenous Graf (AVG) Vascular Access

Sources: (Lok *et al*., 2025)

c. Central Venous Catheter (CVC) Vascular Access

A central venous catheter (CVC) may be classified as either a non-tunneled catheter, which is intended for short-term or emergency use, or a tunneled catheter, which is designed for long-term vascular access (Venegas-Ramírez *et al*., 2025).

One type of CVC is the catheter double lumen (CDL), a hemodialysis catheter with two lumens that is inserted into a central vein. The catheter may be introduced through the femoral vein into the inferior vena cava or through the internal jugular or subclavian vein into the superior vena cava, where it functions as vascular access for hemodialysis. CDL is available in two types: a non-cuffed catheter, which is intended for use for less than three weeks, and a tunneled cuffed catheter, which is recommended for use exceeding three weeks (Khosim & Dewi, 2025). Its use is primarily indicated for patients requiring emergency hemodialysis, particularly when an arteriovenous fistula (AVF) is unavailable or when fistula creation is not feasible (Fresia *et al*., 2024).

Compared with an arteriovenous fistula (AVF), a CDL provides a lower blood flow rate, which may reduce dialysis efficiency (Muslimah et al., 2025). Although it serves as an effective temporary vascular access, long-term use of a CDL is generally discouraged because it is associated with a higher risk of complications, including venous stenosis, catheter-related infections, and thrombosis, owing to both its temporary nature and the catheter insertion procedure (Alwi *et al*., 2024).

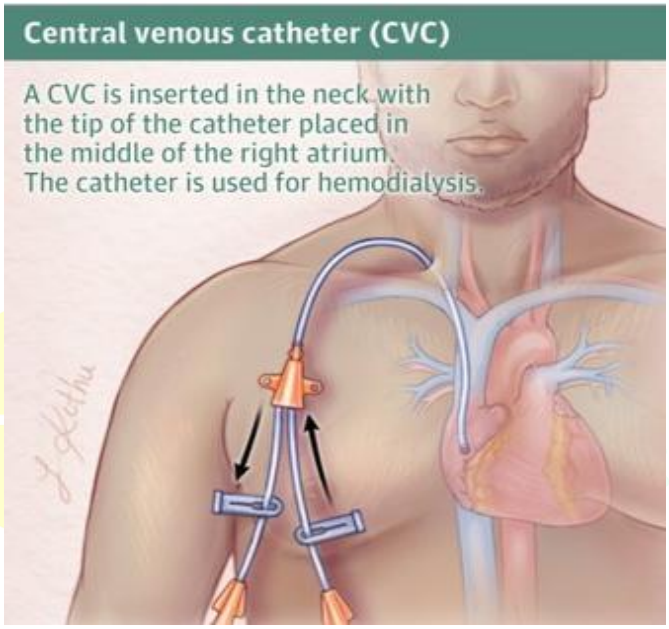

Figure 2.5 Catheter Double Lumen (CDL) Vascular Access

Sources: (Lok *et al*., 2025)

3. Purpose and Function of Vascular Access

During hemodialysis, vascular access serves as the conduit between the patient's bloodstream and the extracorporeal circulation system, enabling efficient blood flow and facilitating the removal of metabolic waste products and excess fluid from the body (Khosim & Dewi, 2025). Beyond its technical role, vascular access also has important prognostic implications, as the type of vascular access is directly associated with patient survival, hospitalization rates, and health-related quality of life (Nousis *et al*., 2025; Venegas-Ramírez *et al*., 2025).

The primary purpose of vascular access placement in patients undergoing maintenance hemodialysis is to establish a reliable, effective, and durable route for extracorporeal blood circulation, allowing blood to be safely withdrawn from the body, filtered through the dialysis system, and returned to the patient. In addition, vascular access is intended to ensure adequate dialysis delivery in accordance with established therapeutic standards and to support long-term treatment planning based on the patient's clinical condition. Accordingly, vascular access functions not merely as a route for blood circulation but as an integral component of the comprehensive management of patients with *end-stage kidney disease* (ESKD). Its selection and maintenance should consider long-term patency, patient safety, the risk of vascular access-related complications, and overall quality of life, thereby contributing to a reduction in hospitalization associated with vascular access complications (Lok *et al*., 2025).

4. Complications of Vascular Acces

Vascular access is a critical component of maintenance hemodialysis because it serves as the primary route for blood circulation between the patient and the dialysis machine. Despite its essential role, vascular access placement is associated with various complications that may adversely affect patients' quality of life and reduce the effectiveness of hemodialysis therapy (Lok *et al*., 2025).

According to Lok *et al*. (2025), the most commonly used vascular access types for patients with chronic kidney disease (CKD) undergoing maintenance hemodialysis include an arteriovenous fistula (AVF), an arteriovenous graft (AVG), and a central venous catheter (CVC), each of which has a distinct complication profile. These complications include the following:

a. Complications of Arteriovenous Fistula (AVF) and Arteriovenous Graft (AVG)
    1) Failure of maturation: AVFs frequently fail to mature (20–60%), rendering them unsuitable for hemodialysis.
    2) Stenosis: Narrowing of the vein, commonly occurring in the *juxta-anastomotic* region of an AVF or at the venous graft anastomosis in an AVG, primarily due to intimal hyperplasia.
    3) Thrombosis: Obstruction of blood flow caused by thrombus formation, which is often secondary to untreated stenosis.
    4) Infection: Less common than in CVCs but may occur, particularly in patients with an AVG.
    5) Aneurysm or *pseudoaneurysm*: Abnormal dilation of the vascular access resulting from repeated cannulation.
    6) *Steal syndrome*: Distal *ischemia* caused by diversion of arterial blood flow through the vascular access, leading to pain, pallor, or ulceration of the affected extremity.
b. Complications of Central Venous Catheter (CVC)
    1) Catheter dysfunction: May result from catheter malposition, kinking, intraluminal thrombosis, or the formation of a fibrin sheath.
    2) Infection: Includes *exit-site infection, tunnel infection,* and *Catheter-Related Bloodstream Infection* (CRBSI), all of which may progress to *sepsis*.
    3) Central venous stenosis: Commonly associated with prolonged CVC use and may lead to venous obstruction and extremity edema.
    4) Vascular rupture: Although uncommon, this complication may be life-threatening.
    5) High-output cardiac failure: A rare but serious complication resulting from the increased hemodynamic burden imposed by the vascular access.

Vascular access complications that are particularly associated with the development of fatigue in patients undergoing maintenance hemodialysis are generally related to inadequate dialysis resulting from impaired vascular access function. Failure of AVF maturation or the presence of stenosis may reduce blood flow, thereby decreasing the clearance of *uremic toxins* and contributing to excessive fatigue. In contrast, the use of a catheter double lumen (CDL) is frequently associated with chronic infection and thrombosis, both of which promote a persistent systemic inflammatory response. This inflammatory state contributes to fatigue, muscle weakness, and reduced energy levels, thereby exacerbating the severity of fatigue. Furthermore, excessively high blood flow through an AVF may result in high-output cardiac failure, which is characterized by dyspnea and easy fatigability due to the increased cardiac workload (Lok *et al*., 2025; Nousis *et al*., 2025; Venegas-Ramírez *et al*., 2025).

E. Association Between Arteriovenous Fistula (AVF) Vascular Access and Fatigue

An arteriovenous fistula (AVF) is a surgically created direct connection between an artery and a vein, typically in the upper extremity. AVF is the preferred vascular access for long-term hemodialysis because of its advantages, including superior patency, a relatively lower risk of infection than tunneled catheters, and higher blood flow efficiency (Segal & Qaja, 2022). Consequently, AVF is widely regarded as the *gold standard* vascular access for hemodialysis due to its lower complication rates, longer access patency, and reduced risk of infection (Lok *et al*., 2025).

Although AVF is more resistant to infection than tunneled catheters, patients remain at risk of blood loss during hemodialysis treatment, particularly during AVF cannulation and access-related complications such as bleeding or leakage. Blood loss may contribute to anemia, which is a major determinant of fatigue because it reduces the oxygen-carrying capacity of the blood, thereby impairing tissue oxygenation (Mailani *et al*., 2025).

Compared with tunneled catheters, AVF provides more stable and efficient blood flow during hemodialysis. Higher blood flow rates facilitate more effective removal of uremic toxins, including urea and creatinine, thereby reducing the uremic burden that contributes to fatigue. However, inadequate AVF maturation or the presence of stenosis may reduce blood flow, resulting in inadequate dialysis and an increased risk of fatigue (Nenova & Yankov, 2025).

Evidence from a study conducted among patients undergoing hemodialysis in South Korea further supports these findings. Patients with AVF demonstrated better survival rates, higher quality-of-life scores, and lower levels of depression than those using central venous catheters (CVCs). Furthermore, fatigue severity was lower among patients with AVF, suggesting that the stability and efficiency of this vascular access contribute to improved dialysis adequacy and better patient outcomes (Kim *et al*., 2020).

Similarly, a study by Nousis *et al*. (2025), reported that patients undergoing hemodialysis with AVF experienced lower fatigue severity than those using other vascular access types, including tunneled catheters, nontunneled catheters, and arteriovenous grafts. Fatigue severity was assessed using the *Fatigue Severity Scale* (FSS), and the *mean* fatigue score in the AVF group was 4.15 ± 1.65, which was significantly lower than that of the tunneled catheter group (4.79 ± 1.25; $p = 0.048$). These findings suggest that the use of AVF not only improves survival among patients with chronic kidney disease but also plays an important role in reducing fatigue and enhancing the quality of life of patients receiving maintenance hemodialysis (Nousis *et al*., 2025).

F. Association Between Catheter Double Lumen (CDL) Vascular Access and Fatigue

A catheter double lumen (CDL) is a type of central venous catheter specifically designed for hemodialysis, consisting of two lumens: an arterial lumen that withdraws blood from the patient's circulation to the dialysis machine and a venous lumen that returns the filtered blood to the patient's circulation. A CDL is commonly used as a temporary or intermediate-term

vascular access, particularly when an arteriovenous fistula (AVF) has not yet matured or when the patient does not have a functional AVF available for use (Lok *et al*., 2025).

Patients receiving hemodialysis through a CDL generally experience greater fatigue severity and poorer quality of life than those using an AVF. This association has been attributed to the higher risk of catheter-related infections, thrombosis, and frequent hospitalization resulting from catheter-related complications, all of which increase both the physical and psychological burden experienced by patients (Venegas-Ramírez *et al*., 2025). Furthermore, patients with a CDL report greater limitations in activities of daily living, particularly bathing and self-care, which further contribute to emotional and social fatigue. Although patients with an AVF may occasionally experience physical complications such as bruising or bleeding, the overall burden of fatigue remains lower than that observed among patients using a CDL (Maguire *et al*., 2022).

A study conducted by Muslimah *et al*. (2025), demonstrated a significant difference in hemodialysis adequacy between patients using a CDL and those using an AVF. The Mann–Whitney test yielded a p-value of < 0.001, indicating a statistically significant difference. Higher dialysis adequacy was observed among patients with an AVF (86.6%) than among those with a CDL (44.8%). The lower dialysis adequacy associated with CDL use contributes to the accumulation of uremic toxins, which is recognized as one of the primary contributors to fatigue among patients with chronic kidney disease (Muslimah *et al*., 2025). Similar findings have been reported in a Korean patient population, where the use of a CDL was associated with higher mortality, poorer health-related quality of life, and more severe depressive symptoms than permanent vascular access modalities. These adverse outcomes may further exacerbate patients' perception of fatigue (Kim *et al*., 2020).

Patients using a CDL, particularly tunneled catheters, have also been reported to exhibit higher *Fatigue Severity Scale* (FSS) scores than those using an arteriovenous fistula (AVF). The *mean* FSS score among patients with

tunneled catheters was 4.79 ± 1.25, compared with 4.15 ± 1.65 among patients with an AVF. Statistical analysis demonstrated a significant difference in fatigue severity according to vascular access type (p = 0.048). These findings suggest that the use of a CDL is associated with more severe fatigue among patients with chronic kidney disease undergoing maintenance hemodialysis (Nousis *et al*., 2025).

G. Theoretical Framework

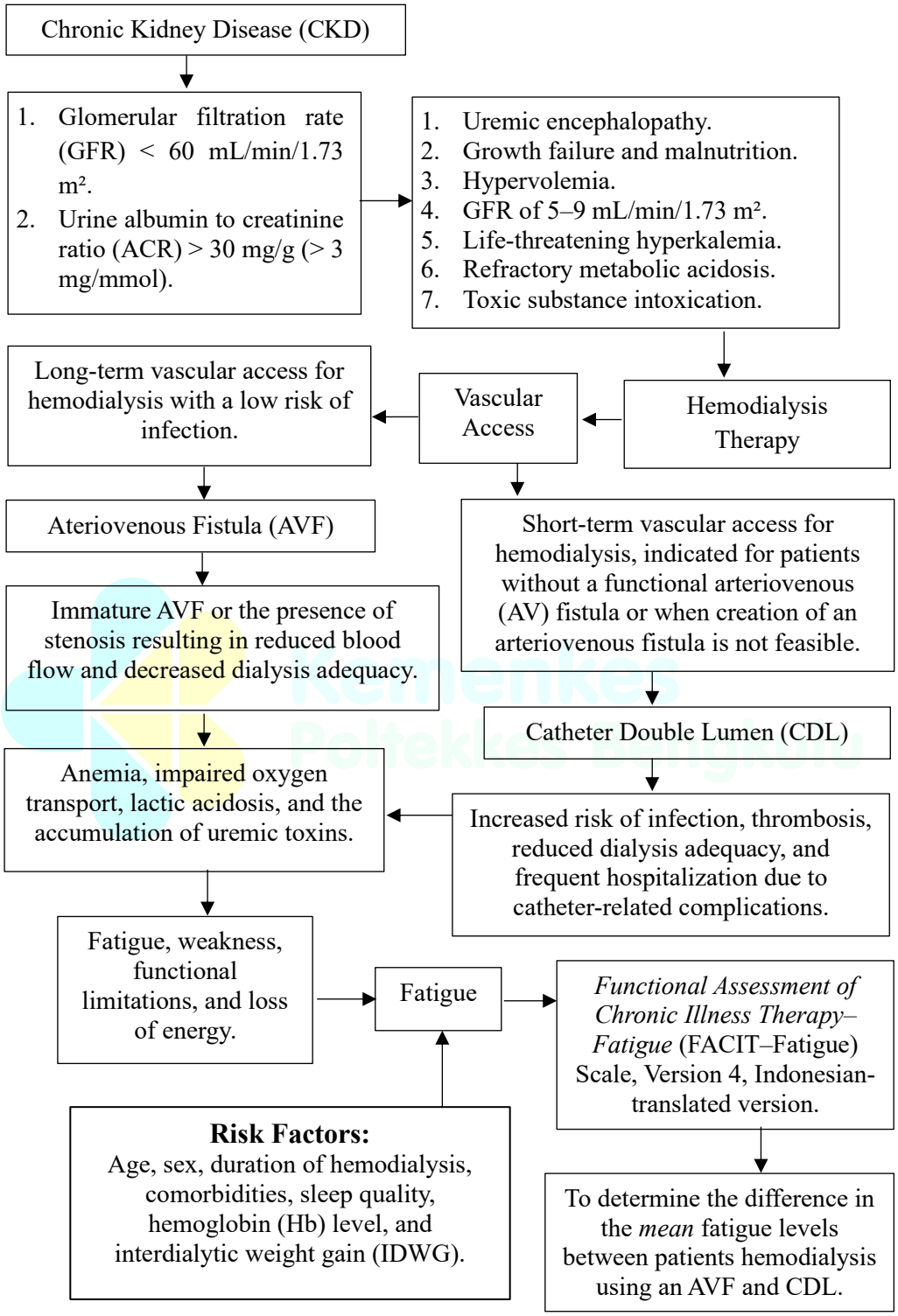

Diagram 2.1 Theoretical Framework

Sources: (Lok *et al*., 2025; Mailani *et al*., 2025; Nousis *et al*., 2025; Sihombing *et al*., 2016; Stevens *et al*., 2024; Tennant, 2019)