Epidemiology of chronic kidney disease and the heightened risk of hepatitis C virus infection in low-resource settings

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Abstract

Chronic Kidney Disease (CKD) is a significant non-communicable disease with varying incidence and prevalence globally. Over the past two decades, it has emerged as one of the leading causes of mortality. In Indonesia, CKD has risen sharply and now represents one of the highest disease-related cost burdens. CKD patients, both men and women, across different age groups, face complex challenges, including the risk of Hepatitis C Virus (HCV) infection due to Hemodialysis (HD). This cross-sectional study investigated 43 CKD patients undergoing HD twice weekly for at least one year at a regional hospital in Yogyakarta, all of whom initially tested negative for HCV. The results revealed that 58.1% of CKD patients were female, with 32.6% aged 55-65 years. Most (60.5%) had completed high school education, and 39.5% were housewives. Interestingly, 69.8% of cases were not primarily caused by kidney-related conditions. Importantly, the longer a patient undergoes HD, the higher their risk of acquiring HCV infection. Although the percentages may vary across different settings, this study highlights the urgent need for targeted infection control measures, particularly in resource-limited healthcare environments where access to preventive strategies may be constrained.

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Introduction

Chronic Kidney Disease (CKD) is a non-communicable disease that has emerged as a significant global health concern, with varying incidence and prevalence rates across regions.[1] Over the past two decades, CKD has become one of the leading causes of death worldwide, affecting more than 10% of the global population, or over 800 million people, as of 2022. In the United States, it is estimated that more than 1 in 7 adults has CKD.[2,3] The National Basic Health Research (Riskesdas) 2018 in Indonesia reported a 2.0% increase in the prevalence of CKD since 2013, making it the fourth most burdensome catastrophic disease in terms of healthcare costs in the country.[4,5]

CKD can affect individuals of all ages, with varying prevalence. In terms of gender and age characteristics, CKD is more commonly observed in women and the elderly.[3] Physiologically, the kidney volume decreases with age, leading to reduced function due to nephrosclerosis, where the number of nephrons decreases by approximately 20% starting at the age of 50.[6,7] The spread of CKD is influenced by demographic factors such as education and employment, which cannot be separated from its complexity. Additionally, cultural habits, such as the consumption of alcoholic beverages (*e.g.*, alcohol, wine, *tuak* [traditional alcoholic drink]), formed since adolescence, and environmental health factors add further challenges.[6-8]

A history of certain diseases also plays a crucial role in the incidence of CKD. Diabetes and hypertension are the most common causes of CKD, rather than diseases originating from the kidneys.[9-11] Hypertension serves both as a causative factor and a consequence of CKD.[12] This is particularly relevant to Hemodialysis (HD), which can lead to increased blood pressure during or shortly after the procedure, a condition known as intradialytic hypertension.[13] HD remains the most widely used life-sustaining therapy for CKD patients.[14,15] While HD has been shown to improve the life expectancy of CKD patients, it also presents risks, particularly the spread of Hepatitis C Virus (HCV) infections.[16,17] The duration of HD therapy significantly increases the risk of HCV transmission among CKD patients.[18,19] This study aims to determine the epidemiological picture of patients with CKD and the risk of HCV transmission due to HD.

Materials and Methods

This research is an observational study with a descriptive, cross-sectional design approach. The data used was secondary data obtained from medical records of hemodialysis patients at Yogyakarta Regional Hospital. The population of this study was non-hepatitis HD patients who were actively undergoing HD procedures twice a week. Inclusion criteria in this study include: i) patients who are actively undergoing HD procedures twice a week; ii) have undergone HD for at least one year; iii) and have non-reactive hepatitis test results. From the population that met the inclusion criteria, 43 patients who were willing to participate in this study were selected. This study has obtained ethical approval from the Health Research Ethics Committee (KEPK) with number 180/5402.13. In addition, this study also obtained official permission from the Director of Yogyakarta Regional Hospital with number 070/5425.30.

Results and Discussion

This study examined several key variables, including gender, age, educational level, occupation, CKD etiology, and the duration of HD treatment. The collected data were analyzed descriptively and presented in tables and narratives based on the studied variables.

Gender and age characteristics

The incidence of CKD in this study was found to be more prevalent in women (58.1%) than in men (41.9%). This finding aligns with data from the 2018 RISKESDAS, which reported that 60.3% of CKD patients in Indonesia were women.[5] Similarly, a study conducted in 2020 at Montaserieh Hospital in Mashhad, Iran, found that out of 1034 CKD patients, 605 were women.[20] Studies in Alberta, Canada, showed that 55.2% of 81,320 kidney failure patients were women,[21] and 50.9% of 225 CKD patients on HD in Karachi, Pakistan, were also women.[19] In 2016, 417 million out of 753 million CKD patients globally were women.[22] The higher prevalence in women is often attributed to better adherence to therapy, complications during pregnancy, autoimmune factors, and differences in dialysis-related complications between genders.[23,24] However, other studies have reported that CKD is more common in men due to lifestyle factors and a higher prevalence of hypertension and diabetes.[25-28] The higher prevalence of CKD in women compared to men can be attributed to a combination of biological, behavioral, and healthcare-related factors. Biologically, women tend to have a lower baseline Glomerular Filtration Rate (GFR) than men, which may predispose them to earlier stages of CKD.[29] Additionally, women are more likely to have comorbid conditions such as hypertension and diabetes, which are significant risk factors for CKD.[30,31] Despite these factors, men are more likely to progress to severe stages of CKD and require kidney replacement therapy, possibly due to a steeper decline in kidney function with age and the influence of androgens, which have pro-apoptotic and pro-fibrotic effects on the kidneys.[29,32] Furthermore, women with CKD are often less aware of their condition, which may delay diagnosis and management, contributing to higher prevalence rates.[33] Healthcare disparities also play a role, as women are less likely to receive timely specialist care and appropriate treatment, such as kidney replacement therapy, compared to men.[30,31] Additionally, lifestyle factors such as higher rates of obesity and poorer adherence to dyslipidemia medications in women may exacerbate CKD progression.[34]

Estrogen and other hormonal effects can impact renal function and the advancement of kidney disease in females. Hormonal variations during pregnancy, menopause, or diseases such as pre-eclampsia can elevate the risk of CKD. Pregnancy-associated disorders such as pre-eclampsia, eclampsia, and postpartum hypertension are substantial contributors to chronic kidney disease in women. Women exhibit a higher susceptibility to autoimmune illnesses such as Systemic Lupus Erythematosus (SLE) and rheumatoid arthritis, which may result in renal impairment or secondary renal injury. Furthermore, the shorter urinary tracts in women render them more vulnerable to Urinary Tract Infections (UTIs), which may result in kidney infections and potentially contribute to CKD over time.

Women are more inclined than men to pursue healthcare and participate in routine tests, resulting in an elevated incidence of CKD diagnoses. This proactive behavior may exaggerate prevalence statistics compared to men who may have undiscovered illnesses due to insufficient healthcare participation. Women typically exhibit superior compliance with prescribed medicines and lifestyle changes, potentially enhancing outcomes while also elevating the probability of early identification and diagnosis of CKD. Women's interaction with healthcare systems significantly affects access to care and diagnosis, particularly during pregnancy and regular reproductive health appointments. Pregnancy-related testing can identify renal complications earlier than males, who often seek healthcare only when unwell. Women on hemodialysis face an elevated risk of complications, including anemia and vascular access problems, which may aggravate the progression of CKD. Cultural and socioeconomic factors can exacerbate CKD risk by exposing women to poor dietary habits, strenuous labor, and circumstances such as early marriages and multiple pregnancies.

Global research indicates that a higher number of women are diagnosed with CKD, whereas men are more prone to advancing to End-Stage Kidney Disease (ESKD). This gap may indicate a slower illness course in women attributable to biological reasons and earlier diagnosis. Nevertheless, when women attain advanced stages of CKD, they frequently encounter inferior results, presumably because of disparities in access to specialized care and treatment. These multifaceted factors collectively contribute to the observed higher incidence of CKD in women compared to men.

Regarding age, CKD in this study occurred predominantly in individuals over 45 years old, accounting for 67.5% of cases, which is double the percentage for patients aged 15-44 years (32.5%). This finding is consistent with 2018 RISKESDAS data, which reported a CKD prevalence of 15.3 per 1000 people aged over 45 years compared to 6.92 per 1000 people aged 15-44 years.[5] A study in Sudan also found the average age of CKD patients on dialysis to be 55 years.[35] This age distribution is closely related to the natural decline in kidney function. Starting at age 30, the Glomerular Filtration Rate (GFR) decreases by approximately 8 mL/minute/1.73 m² per decade. By the age of 40, significant nephron loss begins, further impacting kidney filtration capacity.[36] In younger populations, CKD may arise from congenital kidney and urinary tract abnormalities, as seen in 2.7% of individuals under 29 years, including healthy individuals.[7,37]

CKD mainly occurs in individuals over 45 years old due to a combination of physiological, pathological, and demographic factors. As individuals age, there is a natural decline in kidney function, which is often exacerbated by the presence of chronic conditions such as diabetes, hypertension, and cardiovascular diseases, all of which are more prevalent in older populations.[38,39] The prevalence of CKD increases significantly with age, with studies indicating that more than 45% of adults aged 70 years or older in the

United States are affected by CKD.[40] This age-related increase in CKD prevalence is partly due to cumulative exposure to risk factors over time, including lifestyle factors such as smoking and the use of nephrotoxic medications like NSAIDs.[39,41] Additionally, Acute Kidney Injury (AKI), which is more common in the elderly due to age-related changes in kidney function and the impact of chronic diseases, significantly raises the risk of developing CKD.[18] The physiological changes associated with aging, such as reduced Glomerular Filtration Rate (GFR), are often misinterpreted as pathological, leading to potential overdiagnosis of CKD in older adults.[42,43] Furthermore, the lack of age-adjusted diagnostic criteria for CKD can result in the misclassification of age-related kidney function decline as CKD, contributing to the higher-reported prevalence in older populations.[42,43] The interplay of these factors underscores the importance of age-specific screening and management strategies to accurately diagnose and treat CKD in older adults, thereby preventing progression to end-stage renal disease and reducing associated morbidity and mortality.[44]

CKD is more prevalent in older adults due to a combination of natural aging processes and risk factors. The kidneys inherently diminish some of their filtration capacity due to decreased functioning nephrons and alterations in kidney architecture. Chronic conditions such as diabetes and hypertension are prevalent in older adults, resulting in progressive renal impairment. Prolonged exposure to renal stressors, such as pharmaceuticals, poisons, and infections, may result in enduring damage. Lifestyle variables such as elevated salt or protein consumption, tobacco use, and obesity augment the risk of chronic kidney disease. Older adults are more vulnerable to Acute Kidney Injury (AKI), which may arise from infections, dehydration, or the administration of nephrotoxic medications. Some individuals have a genetic susceptibility to CKD, which may only manifest as they age, especially when accompanied by environmental factors or lifestyle decisions. Chronic kidney disease frequently advances asymptomatically in its initial phases, and in elderly individuals, manifestations may be ascribed to aging rather than renal pathology, permitting its progression to go unrecognized. Consequently, CKD poses a considerable health risk for the elderly population (Table 1).

Sociodemographic factors

Table 2 shows that most CKD patients in this study were high school graduates (60.5%), similar to population data from Sleman Regency in 2020, which reported that 31.79% of the population had a high school education. Research in four hospitals in Jakarta also reported that 43.3% of CKD patients were high school graduates.[25] Housewives accounted for the majority (39.5%) of job types, followed by employees (30.2%), self-employed individuals (14.0%), and farmers (9.3%). A similar study in hospitals in Kendal and Semarang Central Java found that 28.2% of CKD patients were employees.[45] Occupation plays a significant role as a risk factor for CKD due to varying exposures and habits. For example, employees often consume less water and more energy drinks or sodas, which are known risk factors for CKD.[25,45] Field workers exposed to excessive sunlight or those with physically demanding jobs are also at greater risk of dehydration, leading to more concentrated urine and kidney damage.[46] Educational level plays a significant role in the health outcomes and management of patients with CKD. Studies have shown that lower educational attainment is associated with adverse outcomes in CKD patients, including higher risks of mortality, major adverse cardiovascular events, and kidney failure. This association is mediated by factors such as lifestyle habits and biomarkers, highlighting the importance of educational interventions in improving patient prognosis.[47] In the German CKD cohort, low educational attainment was linked to a higher prevalence of diabetic nephropathy and CKD following acute kidney injury, suggesting that education influences disease etiology and progression.[47] Conversely, higher educational levels were paradoxically associated with an increased risk of incident CKD in an Iranian cohort, potentially due to unhealthy lifestyle behaviors prevalent in this demographic.[48]

Education significantly influences the prevalence of chronic kidney disease by affecting health awareness, lifestyle decisions, healthcare accessibility, and risk management. Individuals with higher education levels typically possess a greater awareness of the significance of sustaining a healthy lifestyle, engaging in practices that safeguard renal health, and eschewing detrimental substances such as smoke and excessive alcohol. Health literacy is influenced by education, as those with higher educational attainment are more likely to identify early indicators of kidney failure, seek medical counsel promptly, and comply with medical directives. The early identification of CKD is essential for averting its progression, as it frequently advances unnoticed during its earliest phases. Socioeconomic factors also play a role in access to healthcare, as people with higher education levels have better access to health insurance, routine health check-ups, and financial means to pay for preventive care or treatments. Individuals with lower educational attainment may encounter obstacles in obtaining these resources, hence elevating their risk of undetected or inadequately managed CKD. Chronic disorders such as diabetes and hypertension are substantial risk factors for CKD, and education greatly influences an individual's capacity to comprehend and manage these symp-

Table 1. Characteristics of gender and age.

Characteristics	Frequency	%
(%)		
Gender		
Men	18	41.9
Women	25	58.1
Age (based WHO)		
15-24	1	2,3
25-34	4	9.3.
35-44	9	20.9
45-54	11	25.6
55-64	14	32.6
65-74	3	7.0
≥ 75	1	2.3

Table 2. Sociodemographics.

Sociodemographics	n (43)	%
Educational level		
No school	1	2.3
Primary school	5	11.6
Junior school	5	11.6
High school	26	60.5
Higher education	6	14
Job type		
Housewives	17	39.5.
Employees	13	30.2
Self-employed	6	14
Public-servant	2	4.7
Farmers	4	9.3
Students	1	2.3

toms. Inadequate care of these illnesses in individuals with lower educational attainment elevates the risk of CKD. Behavioral and environmental factors significantly impact diet, exercise, and living situations, hence directly influencing kidney health. Educational attainment is a pivotal factor influencing CKD risk, and mitigating educational inequities with advancing health education is a vital approach to alleviating the CKD burden, particularly among at-risk populations. Educational interventions, such as nurse-led programs and patient information leaflets, have been effective in enhancing CKD patients' knowledge and management skills, leading to improved health outcomes.[49,50] For instance, a nurse-led educational intervention significantly increased patients' knowledge scores, which is crucial for managing CKD and preventing progression to end-stage renal disease.[49] Similarly, group-based education has been shown to effectively reduce body weight and uric acid levels, which are critical factors in CKD management.[51] Moreover, therapeutic patient education has been instrumental in helping patients make informed decisions about renal replacement therapy, with a significant correlation between educational level and knowledge acquisition.[52] These findings underscore the critical role of education in CKD management, suggesting that targeted educational strategies could mitigate the socioeconomic disparities observed in CKD outcomes.[53,54] Therefore, integrating educational interventions into CKD care plans could enhance patient empowerment, improve adherence to treatment regimens, and ultimately lead to better health outcomes.

Etiology of CKD

The results revealed that 69.8% of CKD cases were caused by non-kidney diseases, such as hypertension and diabetes mellitus, while the remaining 30.2% were attributed to kidney-related conditions (Table 3). This is consistent with research in developing countries, where HT and DM are the leading causes of CKD.[55,56] Hypertension damages the kidneys through the thickening of the tunica intima cells in the renal glomerulus, which reduces blood flow and activates the renin-angiotensin-aldosterone system. This leads to a vicious cycle of increased blood pressure and progressive kidney damage.[57] CKD is principally caused by non-kidney diseases such as hypertension and diabetes mellitus, which are the leading contributors to CKD globally. Hypertension is a significant risk factor for CKD due to its role in causing hypertensive nephropathy, which is a common etiology of CKD, as evidenced by studies showing its prevalence in non-diabetic CKD patients.[58,59] Diabetes mellitus, particularly diabetic nephropathy, is the most common cause of CKD worldwide, as it leads to progressive kidney damage through mechanisms such as hyperglycemia-induced glomerular damage.[60,61] In addition to these, obesity and metabolic syndrome, often associated with diabetes, contribute to early signs of kidney disease, further exacerbating the risk of CKD.[62] However, CKD can also arise from kidney-related conditions such as glomerulonephritis and chronic tubulointerstitial nephritis, which are prevalent in Non-Diabetic Kidney Disease (NDKD) cases. For instance, studies have identified membranous glomerulopathy and focal segmental glomerulosclerosis as common histological lesions in NDKD. Environmental factors, such as exposure to insecticides and self-medication with NSAIDs, have also been linked to CKD in populations without traditional risk factors like diabetes and hypertension.[63] Furthermore, in certain regions, CKD of unknown etiology, often linked to environmental toxins and recurrent dehydration, has been observed, highlighting the complex interplay of various factors in CKD pathogenesis.[62] Thus, while hypertension and diabetes are primary drivers of CKD, a spectrum of other kidney-related and environmental factors also contribute significantly to its development. CKD is predominantly induced by extrarenal conditions such as hypertension and diabetes mellitus, which have considerable systemic impacts on the body, including the renal system. Hypertension, a primary contributor to CKD, exerts excessive pressure on the kidneys' fragile blood arteries, compromising their capacity to filter waste and maintain fluid equilibrium. As renal function deteriorates, hypertension frequently exacerbates, establishing a detrimental cycle that accelerates the onset of CKD. Diabetes mellitus, conversely, impairs the kidneys via diabetic nephropathy, resulting in elevated pressure inside the glomeruli, hypertrophy of the glomerular basement membrane, and subsequent fibrosis. The increasing incidence of type 2 diabetes has greatly augmented its role in chronic kidney disease CKD, rendering it the predominant cause of CKD globally. Non-renal disorders such as hypertension and diabetes are widespread, inflicting renal damage over years prior to the manifestation of symptoms, complicating early intervention. They also induce extensive vascular damage, affecting various organs and thereby exacerbating renal results. Kidney-specific disorders, including glomerulonephritis, polycystic kidney disease, and renal infections, are few; however, they can be identified early due to symptomatic presentation. Risk factors include obesity, poor dietary habits, and limited access to preventative healthcare, which elevate the probability of hypertension and diabetes, thus indirectly increasing the prevalence of chronic kidney disease. Addressing these systemic concerns is essential for diminishing global cases of CKD.

Risk of hepatitis C in CKD patients

Patients undergoing HD are at increased risk of hepatitis C virus (HCV) infection due to frequent exposure to contaminated blood products and equipment.[1] The study showed that 62.8% of patients underwent HD for 1-2 years, 25.6% for 3-4 years, and 11.6% for 5-6 years. Prolonged HD is a significant risk factor for HCV transmission, especially in low-resource settings where dialyzers are often reused to minimize costs (Table 4).[64,65]

Extended exposure to dialysis treatments heightens the risk of contact with infected blood or contaminated instruments, as HCV is transferred via blood. Commonly utilized devices, such as blood pressure cuffs and waste disposal zones, may serve as fomites, collecting pathogens through repeated exposure over time. Frequent blood access heightens the danger of inadvertent contamination or

Table 3. Etiology.

Etiology	n (43)	%
Non-kidney disease	30	69.8
Hypertensive (HT)	23	53.5
Diabetes mellitus (DM)	2	4.7
HT and DM	5	11.6
Kidney disease	13	30.2
Total	43	100

Table 4. Length of hemodialysis treatment.

Length of HD (years)	Patients with negative hepatitis	
	n (43)	%
1-2	27	62.8
3-4	11	25.6
5-6	5	11.6
Total	43	100

infection due to violations of aseptic protocols. Transmission between patients happens in dialysis centers with inadequate infection management, especially in environments characterized by overcrowding or limited resources. Immunosuppression in patients with pre-existing renal failure or related diseases increases their vulnerability to infections, including HCV. Insufficient screening for HCV in dialysis patients or donors may result in undiagnosed instances, hence elevating the cumulative risk. Patients who eradicate an HCV infection may nevertheless be susceptible to reinfection due to ongoing exposure in the dialysis setting.

The increased risk of HCV infection with prolonged hemodialysis duration is attributed to several factors inherent to the HD environment and patient management. Hemodialysis patients are particularly vulnerable to HCV due to the invasive nature of the procedure, which often involves repeated vascular access and potential exposure to contaminated equipment or blood products. The longer a patient remains on HD, the greater the cumulative exposure to these risk factors, thereby increasing the likelihood of HCV transmission.[66,67] Studies have shown that the prevalence of HCV infection is significantly higher among patients undergoing chronic dialysis, with rates as high as 58.9% in some cohorts, compared to much lower rates in the general population.[67] This elevated risk is compounded by the frequent need for blood transfusions in HD patients, which, despite screening improvements, still pose a risk for HCV transmission, especially in settings where screening protocols may not be as stringent.[68] Additionally, the use of dialysis catheters, as opposed to arteriovenous fistulas, has been associated with a higher seroconversion rate to HCV positivity, suggesting that the type of vascular access may influence infection risk.[69] Nosocomial transmission within dialysis units is also a concern, as inadequate infection control practices can facilitate the spread of HCV among patients.[68] Furthermore, the immune-compromised status of end-stage kidney disease patients, who are often older and have multiple comorbidities, may exacerbate their susceptibility to infections, including HCV.[66] Therefore, the combination of prolonged exposure to potential sources of infection, the need for frequent medical interventions, and the inherent vulnerabilities of the patient population contribute to the increased risk of HCV infection with longer HD duration.

The correlation between HCV infection rates in hemodialysis patients and the practice of dialyzer reuse is essential for comprehending risk management measures within healthcare systems, particularly in Indonesia. The HCV-negative rates among HD patients reflect the efficacy of infection control measures in dialysis units, demonstrating a higher prevalence in facilities with stringent infection control methods and no dialyzer reuse. The reuse of dialyzers has traditionally been linked to a heightened risk of HCV infection, especially in resource-constrained environments where rigorous sterilization processes may not be consistently implemented. The hospital (research location) has enacted regulations banning the reuse of dialyzers to mitigate the danger of HCV and other blood-borne infections in hemodialysis patients. These laws mandate the use of a new, sterile dialyzer for each patient during every session, thereby mitigating the hazards associated with insufficient sterilization.

To mitigate HCV transmission, strict infection control measures, routine screening, and education are essential. In Indonesia, dialyzer reuse was common until April 2023, when single-use dialyzers were introduced. Previously, dialyzers were manually sterilized with renalin, increasing the risk of cross-contamination.[70-72]

Conclusions

A multifaceted approach, including adherence to universal precautions and effective treatment strategies, is necessary to address this public health concern. To reduce the risk of hepatitis C virus infection among hemodialysis patients in low-resource settings, a multifaceted approach is needed. This includes strict adherence to universal precautions, rigorous hygiene protocols, staff training, routine screening, patient education, and access to effective treatments. Innovative screening strategies and micro-elimination strategies can also help mitigate the long-term consequences of HCV infection.

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