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Original Article

Cancer Incidence in Hemodialysis Patients With End-Stage Renal Disease

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Abstract

Background: The number of individuals undergoing dialysis is rising. Impaired renal function has been linked to a heightened risk of cancer. This study aimed to examine cancer incidence among hemodialysis (HD) patients.

Materials and Methods: This retrospective cross-sectional study analyzed the medical records of individuals with newly diagnosed end-stage renal disease (ESRD) who initiated HD sessions between July 2018 and December 2023 at Urmia Imam Khomeini hospital. The data collected for this study included patient demographics, underlying diseases, malignancy status, and duration of malignancy (less than ten years, 10–20 years, and over 20 years). The obtained data were analyzed using SPSS 21.

Results: The study included 192 patients, with a mean age of 64.45 ± 13.70 years. Of these, 117 (60.9%) were male and 75 (39.1%) were female. The majority of participants (68.8%) resided in urban areas. Hypertension (HTN) was the most common underlying disease (25%), while 32.8% had no reported underlying conditions. Eighteen (9.4%) patients were diagnosed with malignancy, with multiple myeloma being the most prevalent type (43.4%). The remaining 174 (90.6%) patients were not diagnosed with cancer. The onset of malignancy occurred within ten years for the majority of patients (72.2%). No significant association was found between the prevalence of malignancy and patients' age ($P<0.136$) and gender ($P<0.763$).

Conclusion: A significantly elevated incidence of cancer was observed in patients undergoing chronic HD for ESRD, underscoring the critical development of a targeted cancer screening strategy for this vulnerable population.

Keywords: Hemodialysis, Renal failure, Malignancy, Incidence, Patients

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Introduction

Chronic kidney disease (CKD) is a progressive condition that can ultimately lead to end-stage renal disease (ESRD) (1). Individuals with ESRD are at a significantly increased risk of developing cancer compared to the general population (2). Previous studies have extensively investigated the cancer incidence rates in individuals with ESRD, comparing these rates to those observed in the general population (2-4). As life expectancy increases, the worldwide prevalence of CKD and cancer rises (5), making the intersection of these two conditions a significant clinical and socioeconomic concern. Research indicates that impaired renal function, particularly in severe cases, is linked to an elevated risk of certain cancers, especially those affecting the urinary tract (6). Consequently, early cancer detection through timely screening is becoming increasingly crucial (7).

Hemodialysis (HD) currently remains the primary modality of renal replacement therapy for patients with ESRD when kidney transplantation is not a viable option (8). As a result, the number of individuals undergoing maintenance HD continues to rise. Epidemiological studies from diverse geographical regions, including Asia (2, 9), Australia/New Zealand (10), the United States (11), Northern (12), Central (13), and Southern Europe (14), have consistently demonstrated an increased incidence of cancer among individuals undergoing HD for ESRD. However, data on cancer incidence in HD patients from Eastern European countries, such as Romania, where the prevalence of ESRD requiring renal replacement therapy is notably high at 1048 per million population (15), are currently limited. While advancements in cancer treatments, including new medications and supportive care, have significantly improved outcomes (16), the optimal approach for managing cancer in ESRD patients remains uncertain due to the exclusion of these individuals from many clinical trials.

While numerous population-based studies have evaluated cancer incidence in dialysis patients, significant disparities in cancer incidence and the distribution of

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cancer types between this population and the general population remain unclear (17). Furthermore, a notable gap exists in the literature regarding comprehensive cancer incidence data in dialysis populations within many countries. To address this knowledge gap, this study aims to investigate cancer incidence among dialysis patients referred to the Dialysis Center of Urmia Imam Khomeini Hospital in Urmia, Iran.

Materials and Methods

Given the retrospective nature of this study, obtaining written informed consent from participants was not feasible. For this study, individuals with newly diagnosed ESRD who commenced thrice-weekly, four-hour HD sessions between July 2018 and December 2023 were identified from the medical records of patients at Urmia Imam Khomeini Hospital, a leading center for kidney disease treatment, research, education, and training in the southwest of Iran. All patients were enrolled by the census sampling method. Patients were included in the study if they had been receiving maintenance HD for a duration exceeding 90 days.

The collected data included patient demographics (age, gender, and place of residence), underlying diseases, malignancy status, and the duration of malignancy (less than ten years, 10–20 years, and over 20 years) as extracted from patient files.

Inclusion Criteria

- Patients with a diagnosis of ESRD requiring maintenance HD for a minimum duration of three months
- Aged 18 years or older

Exclusion Criteria

- History of kidney transplantation
- Human immunodeficiency virus infection
- Duration of HD treatment less than three months

Statistical Analysis

Quantitative variables were presented as means ± standard deviations, while qualitative variables were expressed as numbers and percentages in appropriate tables and graphs. The chi-square test (or Fisher's exact test when necessary) was employed to analyze and assess the relationship between qualitative variables, and an independent t-test was used to examine quantitative variables. Data analysis was conducted using SPSS 21 software (version 21), and a significance level of less than 0.05 was considered statistically significant.

Results

The age of study participants ranged from 26 to 93 years, with a mean age of 64.45 ± 13.70 years and a median age of 64.5 years (Table 1).

Table 1. Frequency of Studied Variable Among ESRD Patients Undergoing HD

Variable	No. (%)
Mean age (year)	64.45 ± 13.70
Gender	
Male	117 (60.9)
Female	75 (39.1)
Total	192 (100)
Place of residence	
Urban	132 (68.7%)
Rural	60 (31.25%)
Underlying disease	
Yes	129 (67.2)
No	63 (32.8)
High blood pressure	48 (25)
Hypertension and diabetes	39 (20.3)
Hypertension and heart disease	18 (9.4)
Diabetes	12 (6.3)
Diabetes and heart disease	9 (4.7)
Hypertension, diabetes, and heart disease	3 (1.6)
With malignancy	18 (9.37%)
Multiple myeloma	8 (43.4)
Adenocarcinoma of the stomach	3 (16.6)
Kidney cancer	3 (16.6)
Prostate cancer	2 (11.2)
Colorectal cancer	1 (5.4)
Lung cancer	1 (5.4)
Time of occurrence of malignancies	
<10 years	13 (72.2)
10 -20 years	3 (16.6)
>20 years old	2 (1.2)

Note. N: Number; ESRD: End-stage renal disease; HD: Hemodialysis.

Based on the results (Table 1), 192 patients were included in the study, comprising 117 males (60.9%) and 75 females (39.1%). Regarding place of residence, the majority of participants lived in urban areas (68.7%). The most common underlying disease among the study population was hypertension (HTN, 25%), although a significant proportion (32.8%) had no reported underlying diseases. Of the 192 studied patients, 174 (90.6%) were not diagnosed with cancer, while 18 (9.4%) were diagnosed with malignancy. The time of malignancy onset was less than ten years in the majority of patients (72.2%).

Among those with cancer, multiple myeloma was the most prevalent type (43.4%), followed by adenocarcinoma of the stomach (16.6%) and kidney cancer (16.6%), the details of which are displayed in Figure 1.

Independent t-test analysis revealed no statistically significant difference in the prevalence of malignancy between age groups ($P=0.136$, Table 2). Based on the

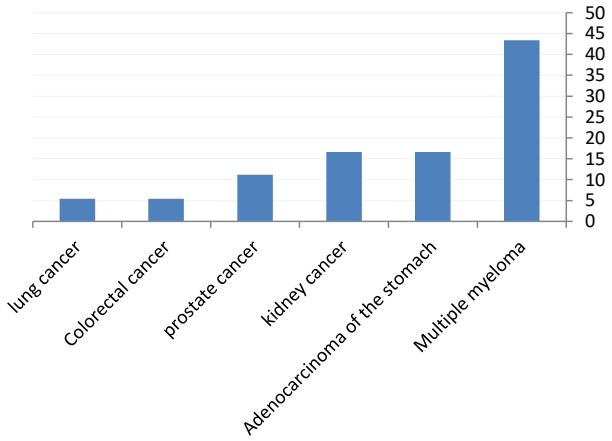

Figure 1. Incidence Curve of the Main Variable (Malignancy)

results of the Chi-square test analysis, no statistically significant association was found between malignancy prevalence and gender ($P=0.763$, $P<0.763$, Table 2).

Discussion

HD, facilitated by specialized devices and materials, has significantly extended the life expectancy of individuals with ESRD (18). However, the rising prevalence of neoplasms in this population has become a major health concern (19). Studies dating back to the late 1990s have consistently reported an elevated risk of cancer among ESRD patients undergoing HD (20). The reported incidence and prevalence rates of cancer in this population exhibit significant variability, ranging from 2.3% (21) to 13.9% across different studies (14), and are influenced by factors such as geographic location, follow-up duration, dialysis treatment length, and gender (3, 22). To address this knowledge gap, this study investigated the incidence of malignancies in a cohort of patients undergoing HD for ESRD.

Individuals undergoing HD for ESRD demonstrate a significantly increased risk of developing cancer compared to the general population (23,24). Several potential mechanisms may contribute to this elevated cancer risk in dialysis patients, which are listed as follows:

- Immunosuppression: Impaired immune function and DNA repair mechanisms in ESRD
- Chronic inflammation: Persistent inflammation associated with CKD
- Medication effects: Potential carcinogenic effects of certain medications used in dialysis therapy
- Environmental factors: Accumulation of uremic toxins and other environmental carcinogens
- Dialysis-related factors: Potential effects of the dialysis procedure itself on cancer development

However, the timing and magnitude of this increased cancer risk remain subject to ongoing debate. Some studies suggest an elevated cancer risk within the first year of dialysis initiation (25, 26), potentially attributed to the unmasking of pre-existing, subclinical malignancies. Nonetheless, other studies, such as a recent nationwide cohort study by Lin et al (19), have demonstrated a higher 7-year cancer incidence rate in dialysis patients compared to matched controls (6.4% vs. 1.7%), suggesting a more sustained period of elevated cancer risk.

Table 2. Prevalence of Malignancies in ESRD Patients Undergoing HD According to Gender and Gender

	With Malignancy	Without Malignancy	*P* Value
Mean age (year)	62.17 ± 12.23	64.69 ± 14.17	<0.136
Gender			
Male	12 (66.7%)	105 (60.3%)	<0.763
Female	6 (33.3%)	69 (39.7%)	

Note. ESRD: End-stage renal disease; HD: Hemodialysis.

Age is a well-established risk factor for cancer development in the general population, and this association is particularly pronounced among individuals with ESRD receiving HD (27). In this study, the patient population revealed a wide age range, spanning from 26 to 93 years, with a mean age of 64.45 ± 13.70 years. The aging of the ESRD population is a significant demographic trend, with a notable increase in the number of older individuals requiring dialysis in recent years (28). Previous research, including studies within the ESRD population, consistently reported an elevated cancer risk in older individuals (29). This increased cancer risk in older adults has been attributed to a variety of factors, including the cumulative effects of chronic inflammation associated with both aging and ESRD (23). However, it is important to note that some studies have identified a heightened risk of de novo cancers even in younger dialysis patients (14, 30), indicating that factors beyond age may contribute to the increased cancer risk observed in this population.

This study comprised a relatively balanced cohort with 60.9% female and 39.1% male participants, which contradicts the global trend of a higher prevalence of ESRD in males (31). While both male and female patients with ESRD represented a significantly increased risk of cancer compared to the general population, regional variations have been detected in cancer risk. Notably, a population-based cohort study conducted in Australia confirmed a significantly increased cancer risk in men with Stage 3 or higher CKD, while this association was not found in women (32, 33). This finding highlights the potential for gender-specific variations in cancer risk within the ESRD population.

The majority (68.8%) of ESRD patients who participated in this study resided in urban areas. This finding is consistent with that of previous research (34), implying the potential for disparities in healthcare access and outcomes between urban and rural populations. Individuals residing in rural areas may experience limited access to specialized healthcare services, including nephrology care and timely management of acute complications such

as cardiovascular events and sepsis (35). This limited access, coupled with potential resource limitations in rural hospitals, may contribute to higher mortality rates among rural ESRD patients compared to their urban counterparts (36). Furthermore, socioeconomic factors can significantly impact healthcare access and outcomes. Individuals residing in low-income urban neighborhoods may face barriers to accessing preventive healthcare services, including regular checkups and early intervention for chronic conditions such as CKD. This lack of access can play a role in the higher prevalence of advanced CKD and ultimately, a higher risk of ESRD (37). Conversely, individuals residing in rural areas with limited access to primary care and nephrology specialists may experience delayed diagnosis and suboptimal management of CKD, increasing their likelihood of progressing to ESRD and experiencing poorer health outcomes (38).

In this study, a significant proportion of patients (32.8%) did not exhibit any identifiable underlying medical conditions. HTN emerged as the most prevalent underlying condition, observed in 25% of the study population. While the association between malignant HTN and kidney damage is well-established, the contribution of non-malignant HTN to the development of ESRD remains less clearly defined. Despite widespread clinical belief, rigorous scientific evidence supporting a direct causal link between non-malignant HTN and ESRD is limited (39). Furthermore, the complex interplay between HTN and kidney disease presents a significant challenge in elucidating the specific role of elevated blood pressure in the progression to ESRD. This is because kidney disease itself can contribute to an increase in blood pressure, making it difficult to isolate the independent effects of HTN on renal function decline (40). Some researchers (40, 41) have proposed that in many cases of HTN-associated ESRD, the underlying etiology may involve primary renal diseases, such as focal segmental glomerulosclerosis, rather than HTN itself being the sole or primary driver of kidney dysfunction.

Of the 192 patients included in the study, 174 (90.6%) did not have a cancer diagnosis, while 18 (9.4%) were diagnosed with malignancy. Among the patients with cancer, multiple myeloma revealed the highest prevalence (43.4%). The spectrum of cancer types observed in this study cohort aligns with the findings of previous research in the ESRD population (3, 17, 24). It is important to note that certain malignancies, such as multiple myeloma and lymphoma, can directly contribute to the development of kidney dysfunction and subsequent progression to ESRD. The reported prevalence of renal involvement in patients with these hematological malignancies ranges from 7% to 34% (42). Prior studies demonstrated an increased incidence of digestive tract cancers, particularly in younger individuals with CKD (43). Further, gender disparities in cancer incidence have been observed within the ESRD population. A study reported colorectal cancer as the most frequent malignancy in men, followed by liver, stomach, lung, and kidney cancers. In contrast, colorectal, breast, thyroid, and stomach cancers were the most prevalent malignancies identified in women with ESRD (44).

The majority of malignancies in our study cohort were diagnosed within ten years following the initiation of HD (72.2%). In line with these findings, the results of previous research represented a relatively short interval between the initiation of dialysis and the development of cancer. A study conducted on Eastern European HD patients confirmed a cumulative cancer incidence of 6.89%, with a median time to cancer diagnosis of approximately one year (range: 0–2.75 years) from the commencement of dialysis (45). Similarly, another study reported a median time to cancer diagnosis ranging from 2.5 to 3.4 years following the initiation of dialysis therapy (3).

Limitations of the Study

This study was limited by its inability to assess cancer-related mortality and survival among the study population. The retrospective design of the study may have introduced potential biases. The exclusion of patients who had undergone kidney transplantation may have limited the generalizability of our findings. Previous research demonstrated an increased risk of malignancies and mortality in kidney transplant recipients (46).

Conclusion

This study highlights a significant burden of cancer within the HD population, emphasizing the importance of early cancer detection and management in this vulnerable patient group. Cancer constitutes a major contributor to all-cause mortality in patients receiving HD. Given the observed cancer incidence in our study population, the development and implementation of a localized cancer screening program specifically tailored to the needs of HD patients is urgently warranted.

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Authors' Contribution

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Writing–original draft: Farhad Behzadi.
Writing–review & editing: Farhad Behzadi.

Competing Interests

The authors have no competing interests to declare that are relevant to the content of this article.

Ethical Approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Urmia University of Medical Sciences (No. IR.UMSU.HIMAM.REC.1401.046).

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