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ORIGINAL

# Demographic and clinical factors associated with kidney disease in oncohematological patients

## Factores demográficos y clínicos asociados a la enfermedad renal en pacientes oncohematológicos

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## ABSTRACT

**Introduction:** the life expectancy of patients with oncohematological diseases is increasing, and there is an increasing likelihood that these malignancies coexist with varying degrees of renal involvement. The incidence of oncohematological diseases, as well as the morbidity and mortality they cause, make it a health problem that requires the adoption of specific measures aimed at raising awareness of the problem, identifying it early, developing guidelines for action in accordance with current knowledge, and facilitating their application in healthcare practice.
**Objective:** to describe the factors associated with the progression of kidney disease in oncohematological patients.
**Method:** an observational, descriptive, longitudinal, and prospective study was conducted in the hematology department of the "Abel Santamaría Cuadrado" General Teaching Hospital in Pinar del Río from May 2020 to May 2022, with 53 patients. Descriptive and inferential statistics were used to display qualitative and quantitative variables.
**Results:** in the present study, it was observed that among oncohematological patients with kidney disease, male sex, white race, and age between 58 and 67 years predominated. Multiple myeloma was the most frequent oncohematological disease and the one associated with the need for hemodialysis. The use of etoposide was associated with the need for hemodialysis treatment.
**Conclusions:** both the diagnosis of multiple myeloma and the use of etoposide are factors associated with the progressive deterioration of kidney disease.

**Keywords:** Chronic Kidney Disease; Oncohematological Disease; Hemodialysis.

## RESUMEN

**Introducción:** cada vez es más alta la esperanza de vida de los pacientes con enfermedades oncohematológicas y más posibilidades de que estos procesos malignos coexistan con diversos grados de afectación renal. La incidencia de las enfermedades oncohematológicas; así como la morbilidad y mortalidad que ocasionan la convierten en un problema de salud que requiere la adopción de medidas específicas, dirigidas a tomar conciencia del problema, identificarlo precozmente, desarrollar pautas de actuación de acuerdo con los conocimientos actuales y facilitar su aplicación en la práctica asistencial.
**Objetivo:** describir los factores asociados al progreso de le enfermedad renal en pacientes oncohematológicos.
**Método:** se realizó un estudio observacional, descriptivo, longitudinal y prospectivo en el servicio de hematología del Hospital General Docente "Abel Santamaría Cuadrado" de Pinar del Río durante el período comprendido entre mayo 2020 y mayo 2022, con 53 pacientes. Se empleó la estadística descriptiva e inferencial para mostrar las variables cualitativas y cuantitativas.
**Resultados:** en el presente estudio se observó que entre los pacientes oncohematológicos con enfermedad

renal predominó el sexo masculino, raza blanca y la edad entre 58 y 67 años. El Mieloma múltiple fue la enfermedad oncohematológica más frecuente y la que mostro asociación a la necesidad de hemodiálisis. El uso de Etopósido se asoció a la necesidad de tratamiento con hemodiálisis.
**Conclusiones:** tanto el diagnóstico de Mieloma múltiple como el uso de etopósido son factores que se asocian al deterioro progresivo de la enfermedad renal.

**Palabras clave:** Enfermedad Renal Crónica; Enfermedad Oncohematológica; Hemodiálisis.

## INTRODUCTION

### Background and current status of the topic

Onconefrology is a new subspecialty of nephrology that recognizes the important intersections of kidney disease and cancer. This intersection takes many forms and includes drug-induced nephrotoxicity, electrolyte disorders, paraneoplastic glomerulonephritis, and the interactions of chronic kidney disease with cancer. Among the neoplasms that have been linked to kidney disease are hematological neoplasms.

Oncohematologic disorders are a group of neoplastic diseases that affect the various cell types involved in the hematopoietic system.[1] These neoplasms include non-Hodgkin lymphomas (NHL), Hodgkin lymphomas (HL), multiple myeloma (MM), acute leukemias (AL), chronic lymphocytic leukemia (CLL), myelodysplastic syndromes/chronic myelomonocytic leukemia (MDS/CMML), chronic myeloproliferative syndromes (CMPS), and others.[2] The first three are the most common.

Leukemia originates from an uncontrolled increase in blood cells and/or bone marrow. In lymphoma, this proliferation occurs in the lymph nodes, and in multiple myeloma, it occurs in the antibody-producing plasma cells of the bone marrow. All of these conditions are hematological cancers and are treated by hematologists.[3]

In Europe, hematological neoplasms are one of the most common causes of cancer.[4] In Spain, the median age of patients at the time of cancer diagnosis is 65, which increases the risk of developing complications with other diseases such as acute kidney failure (AKF).[5] According to the EPIRCE epidemiological study, one in four patients over the age of 65 already has stage 3-5 chronic kidney disease (CKD), which can affect the treatment and progression of the neoplasm. Therefore, kidney disease and cancer share areas of mutual influence: cancer can affect the kidney, either through glomerular lesions or as a result of the toxic impact of chemotherapy; conversely, patients who require renal replacement therapy with dialysis or kidney transplantation have an increased risk of cancer due to the associated immunosuppression diagnosed in the early stages. Non-Hodgkin lymphomas are more common and comprise a wide range of diverse pathologies, some potentially curable (between 10-20 %) and others more complex.[6]

The current approach to classifying leukemia is based on the 2016 World Health Organization (WHO) system. The WHO classification is based on a combination of clinical, morphological, immunophenotypic, and genetic characteristics, classifying them as: acute myeloid leukemia; acute lymphoblastic leukemia; chronic myeloid leukemia; chronic lymphocytic leukemia; and others. Leukemias are also often classified as acute or chronic, depending on the percentage of blasts or leukemic cells in the bone marrow or blood; myeloid or lymphoid, depending on the predominant lineage of malignant cells.[8]

Symptoms vary depending on the type of leukemia. The most common are fatigue, loss of appetite and weight, fever and night sweats; weakness, dizziness or lightheadedness, breathing difficulties, recurrent infections, easy bruising, frequent bleeding from the nose and gums; enlarged lymph nodes and stomach pain or bloating. Other general symptoms may include bone pain, anemia, skin spots (petechiae), and sporadic bleeding.[9]

Lymphomas are malignant tumors of the lymph nodes, or more precisely, the tumorous transformation of lymphocytes, which are the main cells of the lymph nodes. They usually present with a progressive enlargement of the lymph nodes (, some of which can be felt in the neck, armpits, or groin) and fever, night sweats, or unexplained weight loss. Overall, they affect 1 in 5 000 people worldwide.[10] Most cases have a high chance of cure if diagnosed and treated early.

They are classified as Hodgkin's and non-Hodgkin's, with different prognoses and treatments. Hodgkin's lymphoma has a peak incidence in young adults and another in elderly patients and is curable in 80 to 90 % of cases. Among the symptoms, the first thing that can be observed is the growth (usually painless) of one or more lymph nodes. It is important to pay attention to the persistent presence of other symptoms associated with lymphomas, without any other reason to explain their appearance: night sweats, temperature rise to 38 degrees at night, weight loss, chills, fatigue, lack of energy, loss of appetite, cough, persistent itching all over the body and/or rashes, shortness of breath, and headache.[12]

Multiple myeloma accounts for 1 % of all cancers and 13 % of hematological cancers. Its incidence increases progressively with age, peaking between the ages of 50 and 70, and it rarely occurs before the age of 35. Some cases die within a few weeks of diagnosis, while others live for more than ten years.[13]

Diagnosing multiple myeloma is not easy. It often goes unnoticed by primary care physicians, as its symptoms are very similar to those of other diseases such as the flu, bone fractures, anemia, and constipation, among others. Some patients have no symptoms; others may have several, such as frequent urination, thirst, dehydration, kidney problems, abdominal pain, loss of appetite, bone pain, fractures, osteoporosis, and weakness.[14]

Kidney involvement in hematological neoplasms is common. Acute kidney failure (AKF) occurs in up to 60 % of patients and the etiology is varied. On the other hand, the development of chronic kidney disease (CKD) is multifactorial and determines the prognosis of the disease. In addition, improved survival with the advent of new cancer therapies increases the prevalence of patients with CKD.[15]

To assess renal function in cancer patients and determine whether they have any degree of CKD, glomerular filtration rate (GFR) should be evaluated. According to KDIGO guidelines, CKD is defined as the presence of a structural or functional renal abnormality (sediment, imaging, histology) that persists for more than 3 months, with or without impaired renal function; or a GFR < 60 ml/min/1,73 m2 without other signs of kidney disease.[16]

The CKD-EPI (Chronic Kidney Disease-Epidemiology Collaboration) equation uses standardized creatinine methods, providing greater accuracy and predictive capacity of GFR, as well as predicting overall and cardiovascular mortality or the risk of developing end-stage CKD. This equation has shown superiority over others based on serum creatinine concentration (MDRD), cystatin C, or a combination of both. In conclusion, its use is recommended.[17]

Acute kidney injury (AKI) is a common complication in hospitalized patients, but especially in cancer patients undergoing chemotherapy. The incidence of AKI in patients with hematological malignancies reaches 68,5 % using the RIFLE criteria (risk, injury, failure, loss of function, end-stage kidney disease). AKI is defined as a sudden deterioration in kidney function that leads to loss of electrolyte control, acid-base status, and fluid balance, with subsequent accumulation of nitrogenous waste products that should be eliminated by the kidneys. For diagnosis, the Kidney Disease Improving Global Outcomes (KDIGO) guidelines suggest any of the following: a) an increase in serum creatinine of ≥0,3 mg/dl within 48 hours; or b) an increase in serum creatinine of ≥1,5 times the baseline value, known or presumed to have occurred within the last seven days, or c) a decrease in urine output of <0,5 ml/kg/h for six hours. Based on these criteria, patients can be classified according to the severity of their injuries.[18]

Kidney damage in hematological neoplasms may be due to the neoplasm itself or to cancer treatments, and the lesions can affect any renal compartment. The etiology of kidney damage secondary to the neoplasm itself is diverse and can be classified according to the segment of the nephron affected.

- Vascular lesions: due to vascular occlusion caused by disseminated intravascular coagulation or hyperleukocytosis, or renal vein thrombosis.
- Glomerular lesions: the glomerulus may be affected by the appearance of various forms of glomerulonephritis, such as minimal change glomerulonephritis (more common in LH), focal segmental glomerulosclerosis, or membranoproliferative glomerulonephritis.[19]
- Proximal tubule lesions: acute tubular necrosis, lysochymuria, hypercalcemia, nephrocalcinosis, and Fanconi syndrome are very common.
- Tubulointerstitial lesions: common in interstitial lymphoid infiltration, radiation nephropathy, and hemophagocytic lymphohistiocytosis with acute interstitial damage.
- Lesions in the collecting tubules: as in tubular obstruction by paraproteins such as in multiple myeloma, in uric acid nephropathy (usually associated with tumor lysis syndrome), or in BK virus nephropathy.[20]
- Obstructive uropathy due to retroperitoneal adenopathies.
- In addition, these patients are at risk of AKI, such as volume depletion, sepsis, and other comorbidities, especially in elderly patients, such as hypertension, diabetes mellitus, congestive heart failure, etc.[21]

Renal injury may be a direct consequence of the underlying hematological condition. For example, in the case of lymphoma infiltration or extramedullary hematopoiesis, it may be caused by a tumor product; in the case of cast nephropathy, it may be due to the presence of monoclonal immunoglobulin; or it could be due to tumor complications, such as hypercalcemia.[22]

Kidney damage can also be caused by cancer treatment, as many chemotherapy drugs are nephrotoxic. High-intensity treatments, such as high-dose chemotherapy followed by hematopoietic stem cell transplantation, not only increase the risk of infection but can also cause kidney injury through various mechanisms, including viral nephropathies, graft syndrome, and sinusoidal obstruction syndrome. Some conditions, such as thrombotic microangiopathy, may also result directly from the hematologic condition or treatment. New immunotherapies, such as immune checkpoint inhibitors and chimeric antigen receptor T-cell therapy, may also be nephrotoxic. As new therapies for hematologic malignancies with greater antitumor efficacy and lower toxicity are developed, the number of patients receiving these treatments will increase. Clinicians should have a good understanding of the different mechanisms of renal injury associated with cancer to provide better care for these patients.[22]

The clinical management of these entities is highly variable. In general, cancer treatment is oriented toward multiple therapies that minimize treatment-related toxicity (both acute and residual) while maintaining high levels of efficacy. Most hematological malignancies require high-dose chemotherapy, often followed by autologous hematopoietic stem cell transplantation. However, in recent years, the arrival of new antineoplastic agents is providing greater antitumor efficacy with reduced toxicity, which is increasing survival rates for many hematological neoplasms, meaning that the number of patients receiving these therapies will gradually increase.[23]

In order to choose the most appropriate treatment, whether during the induction or maintenance phase, it is vitally important to always take into account the patient's age, medical history, and cytogenetic and molecular characteristics. Thanks to the discovery of new chromosomal regions, new treatments have been developed that often allow targeted therapy to be administered to affect as few healthy cells as possible and are therefore much better tolerated.

Due to the advent of new lines of treatment for oncohematological diseases, the life expectancy of these patients is increasing, as is the likelihood that these malignant processes will coexist with varying degrees of renal involvement. The incidence of these diseases, as well as the morbidity and mortality they cause, make them a health problem that requires early identification of the, demographic, and clinical factors associated with kidney disease in oncohematological patients. In order to improve care and make a timely diagnosis, the following scientific problem has been raised.

### Scientific problem

What are the demographic and clinical factors associated with kidney disease in oncohematological patients?

### Subject

Demographic and clinical factors associated with kidney disease in oncohematological patients.

### Objectives

#### *General objective*

To describe the demographic and clinical factors associated with kidney disease in oncohematological patients.

#### *Specific objectives*

- Characterize the sample according to sex, age, and skin color.
- Show the frequency of kidney disease at diagnosis, taking into account the oncohematological disease present.
- Estimate the association between oncohematological disease and the medication used to treat it, with the need for hemodialysis.
- Show the clinical evolution of patients with kidney disease in the sample studied.
- Identify the possible relationship between the type of oncohematological disease and death.

## METHOD

### General

An observational, descriptive, longitudinal, and prospective study was conducted in the hematology department of the Abel Santamaría Cuadrado General Teaching Hospital in Pinar del Río during the period from May 2020 to May 2022.

### Universe

The universe consisted of patients over 18 years of age, of both sexes, with oncohematological diseases who were admitted to the Hematology ward and developed some type of kidney disease at the Abel Santamaría Cuadrado General Teaching Hospital between May 2020 and May 2022.

### Study population

The study population consisted of 53 patients with complete medical records.

### Sample

Coincided with the universe.

### Exclusion criteria

Patients with incomplete medical records.

**Methods of obtaining information**

*1. Theoretical methods*

Documentary analysis was performed on the bibliography consulted, results of complementary tests, reference texts for the object of study, and individual medical records corresponding to the period in which the research was conducted.

- Analysis and synthesis: used as a dialectical pair throughout the research process, these allowed us to establish mental procedures by which all aspects of the complex are broken down into their various parts and qualities and then reassembled to discover the essential relationships and general characteristics of these, enabling the systematization of knowledge.
- Induction-deduction: this is a procedure whereby, based on the facts observed about acute renal failure in certain areas in a unique way, it is possible to make generalizations based on the previous response and deductive inference throughout the research process, which constitute premises according to the laws of logic.
- Systemic structural: establishes the logical relationship between the elements and the research process, setting the rules and sequences for the development of the phenomenon.

*2. Empirical method*

The medical records of the affected patients were used, and a database was created in order to prepare dynamic tables for processing the data.

The medical records of the patients were analyzed to obtain data such as personal medical history, treatment received, creatinine values, and progression.

To assess renal function in cancer patients and whether they have any degree of chronic kidney disease, glomerular filtration rate (GFR) was evaluated. According to the KDIGO (Kidney Disease Improving Global Outcomes) guidelines, chronic kidney disease is defined as the presence of a structural or functional renal abnormality (sediment, imaging, histology) that persists for more than 3 months, with or without impaired renal function; or a GFR < 60 ml/min/1,73 m2 without other signs of kidney disease.

The CKD-EPI (Chronic Kidney Disease-Epidemiology Collaboration) equation uses standardized creatinine methods, providing greater accuracy and predictive capacity of glomerular filtration for overall and cardiovascular mortality or the risk of developing end-stage CKD. This equation has shown superiority over others based on serum creatinine concentration (MDRD), cystatin C, or a combination of both. In conclusion, its use is recommended.

Acute kidney injury is a concept within chronic kidney disease and is defined as a doubling or more of the baseline creatinine level, which was previously altered.

The parameters for stratifying acute renal failure were established as the diagnostic criteria, based on the relative elevation of serum creatinine relative to baseline.

To determine the evolution of the patients in the study, creatinine levels were measured at 3 months after admission, and patients who died during the study period were also taken into account.

*3. Statistical Methods*

For the statistical analysis of this information, and given its characteristics, the final results were processed and presented in distribution and frequency tables, with absolute frequency and percentage value as units of measurement for better understanding.

**Operationalization of variables (table 1)**

**Table 1.** Operational variables

| Variable | Classification | Scale | Indicator, summary measure |
|---|---|---|---|
| Sex | Qualitative<br>Nominal<br>Dichotomous | Female<br>Male | Absolute and relative frequency percentage |
| Age | Quantitative<br>Continuous<br>Discretized into groups | Years: 18-27, 28-37, 38-47, 48-57, 58-67, 68-77, 78 and over | Absolute and relative frequency percentage |
| Skin color | Qualitative nominal<br>Polytomous | Black and white | Absolute and relative percentage frequency |
| Type of kidney damage at diagnosis | Qualitative nominal<br>Polytomous | Acute renal failure (ARF)<br>Chronic kidney disease (CKD)<br>Acute exacerbation of chronic kidney disease (acute CKD) | Absolute and relative frequency percentage |

| | | | |
|---|---|---|---|
| Oncohematological diseases | Nominal qualitative Polytomic | Multiple myeloma, non-Hodgkin lymphoma, Hodgkin lymphoma, Chronic Myeloid Leukemia, Chronic lymphocytic leukemia | Absolute and relative percentage frequency |
| Need for hemodialysis | Qualitative Nominal Dichotomous | Yes No | Absolute and relative frequency percentage |
| Medication | Qualitative Nominal Dichotomous | Dexamethasone, Prednisone, Vincristine, Adriamycin, Citisor Cisplatin, Etoposide, Cyclophosphamide, Thalidomide, Hydroxyurea, Bleomycin, Ac Soledronium | Absolute and relative frequency |
| Progression of patients with kidney disease | Nominal qualitative Polytomic | IRA recovered CKD stages 3, 3b, 4, 5 Deceased | Absolute and relative frequency percentage |
| Deceased | Qualitative Nominal Dichotomous | Yes No | Absolute and relative frequency percentage |

**Statistical processing**

The information obtained was stored in a spreadsheet created with Microsoft® Excel 2010 software and processed with version 22 of SPSS running on Windows XP.

For the statistical analysis of this information, and given its characteristics, the final results were processed and presented in distribution and frequency tables.

The data were described using aggregation statistics (percentages). For inferential statistics, tests based on the chi-square distribution were applied after distributing the values in a 2 x 2 contingency table. To determine the strength of the association, the corresponding odds ratio (OR) was calculated as a measure of association and its confidence interval. In all cases, an association was considered significant when the p-value was ≤ 0,05.

**Ethical aspects**

This research complied with the basic ethical principles of the research process. It was supported by scientific information based on evidence. A research project was drawn up, discussed, and approved by the Scientific Council and its corresponding Ethics Committee. All data obtained were used for strictly professional purposes, respecting the identity and confidentiality of the information collected.

## RESULTS AND DISCUSSION

This study analyzed information collected from patients over 18 years of age with oncohematological diseases who presented some type of kidney disease. The results related to age and sex are shown below figure 1.

| Edad (años) | Femenino | | Masculino | | Total | |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % |
| 18-27 | 2 | 3.8 | 1 | 1.9 | 3 | 5.7 |
| 28-37 | 1 | 1.9 | 1 | 1.9 | 2 | 3.8 |
| 38-47 | 3 | 5.7 | 7 | 13.2 | 10 | 18.9 |
| 48-57 | 1 | 1.9 | 7 | 13.2 | 8 | 15.1 |
| 58-67 | 6 | 11.3 | 8 | 15.0 | 14 | 26.3 |
| 68-77 | 2 | 3.8 | 6 | 11.3 | 8 | 15.1 |
| 78 y más | 5 | 9.4 | 3 | 5.7 | 8 | 15.1 |
| Total | 20 | 37.8 | 33 | 62.2 | 53 | 100 |

**Figure 1.** Distribution by age and sex of patients treated in the Hematology ward with some type of kidney disease at the Abel Santamaría Cuadrado General Teaching Hospital, 2020-2022

When analyzing the demographic variables of age and sex, it was observed that the most predominant sex was male, with a total of 33 patients (62,2 %), and the most predominant age group was between 58 and 67 years, with a total of 14 patients (26,3 % of the total), followed by patients between 38 and 47 years of age.

Men and the 58-67 age group predominated in the sample. This could be related to the greater predisposition of older people to both neoplastic diseases and some degree of kidney disease, which is largely associated

with the cumulative effect of poor habits and lifestyles that also contribute to the onset of chronic non-communicable diseases such as diabetes mellitus and high blood pressure, which are the main causes of chronic kidney disease and strongly associated with the onset of neoplasms.

The EPIRCE study conducted by the Spanish Society of Nephrology in Spain found that 23 % of patients over the age of 65 had chronic kidney disease (CKD) grades 3-5. Therefore, in terms of age-specific prevalence alone, there is a correlation between cancer and chronic kidney disease (CKD) that explains the large number of consultations between oncology and nephrology departments and justifies the creation of this working group.[24]

Myeloma accounts for around 1 % of all neoplasms and 13 % of hematological cancers; however, its epidemiological pattern is unclear and its causes unknown. The average age at diagnosis is 68 years.[25]

Lymphomas rank fifth among the most common malignant tumors. Hodgkin's lymphoma has a bimodal presentation, with one peak in young adults and another around the age of 65. Non-Hodgkin's lymphoma occurs mainly between the ages of 60 and 70.[26]

The race of the patients included in the study was also studied, and the results are shown in figure 2.

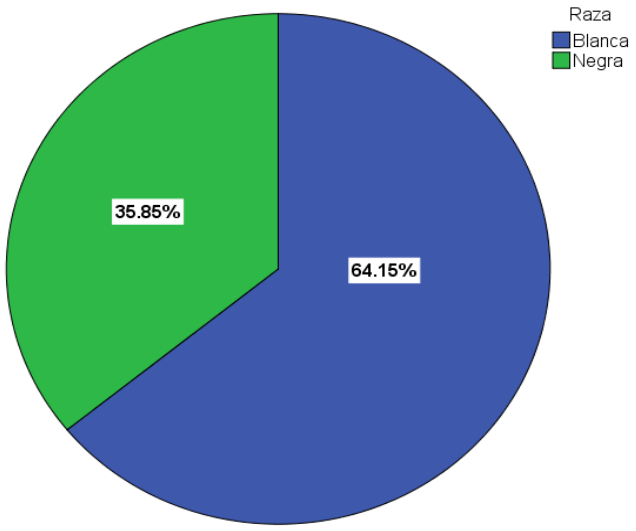


**Figure 2.** Distribution by skin color of patients treated in the hematology ward with some type of kidney disease at the Abel Santamaría Cuadrado General Teaching Hospital, 2020-2022

Figure 2 shows a predominance of white patients, representing 64,15 % of the sample studied. Several studies show a predominance of white patients with some degree of chronic kidney disease (CKD).[27,28] Others differ from these results, highlighting a higher incidence in black individuals.[29,30] With regard to multiple myeloma, a study conducted in Colombia in 2018 by Escobar suggests that it occurs twice as often in black people as in white people, which is not consistent with the results presented here.[31] The frequency of the oncohematological diseases studied in relation to existing kidney damage at diagnosis is shown in figure 3.

| Enfermedad oncohematológica | Enfermedad renal | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | ERC | | ERC agudizada | | IRA | | Total | |
| | No. | % | No. | % | No. | % | No. | % |
| Mieloma múltiple | 4 | 7.5 | 14 | 26.4 | 6 | 11.3 | 24 | 45.3 |
| Linfoma no Hodgking | 5 | 9.4 | 3 | 5.7 | 5 | 9.4 | 13 | 24.5 |
| Leucemia mieloide crónica | 3 | 5.7 | 2 | 3.8 | 3 | 5.7 | 8 | 15.1 |
| Leucemia linfoide crónica | 0 | 0.0 | 2 | 3.8 | 2 | 3.8 | 4 | 7.5 |
| Linfoma Hodgking | 1 | 1.9 | 0 | 0.0 | 3 | 5.7 | 4 | 7.5 |
| Total | 13 | 24.5 | 21 | 39.6 | 19 | 35.8 | 53 | 100.0 |

**Figure 3.** Frequency of kidney disease at diagnosis taking into account the hematological malignancy present.

Figure 3 shows that the hematological malignancy with the highest frequency among patients with kidney damage was multiple myeloma (45,3 %), and acute chronic kidney disease (CKD) was the most prevalent kidney damage among them, at 39,6 %. In patients with Hodgkin's lymphoma, acute kidney injury (AKI) was the most commonly observed kidney damage.

Hematopoietic tissue neoplasms constitute a broad heterogeneous group of pathologies that include

lymphomas, leukemias, lymphoproliferative neoplasms, mast cell neoplasms, plasma cell neoplasms, histiocytic tumors, and dendritic cell neoplasms. In this study, the most common oncohematological disease among patients with kidney damage is multiple myeloma, with acute chronic kidney disease being the most common kidney damage in these patients.

The bidirectional relationship between cancer and kidney disease is complex. Cancer patients, particularly those with hematological neoplasms such as multiple myeloma and lymphoma, are at high risk of developing acute kidney failure, chronic kidney disease (CKD), and/or exacerbation of CKD. On the other hand, there is growing evidence from large observational registries that have consistently shown that the risk of cancer increases at least 2 to 3 times in patients on dialysis and with mild or moderate chronic kidney disease (CKD). The interactions between cancer and chronic kidney disease (CKD) have posed significant challenges in the management of these patients.[32]

Multiple authors have investigated and demonstrated the association between cancer and kidney damage, whether secondary to cancer or as a consequence of the treatments used.[33,34,35,36]

Multiple myeloma is a disease that targets the kidneys. Kidney damage from this disease is mainly due to the toxic effects of monoclonal free light chains. Light chain nephropathy (myeloma kidney) is the most common form of kidney disease associated with multiple myeloma (approximately 90 % of cases).[31]

A study of the population of Pinar del Río conducted at the León Cuervo Rubio Surgical Hospital (2019) in patients with multiple myeloma revealed that the main comorbidities and complications were anemia and renal failure.[37]

The study found that acute chronic kidney disease (CKD) was the most prevalent in the sample, at 39,6 %, being more frequent in patients with multiple myeloma, while in patients with Hodgkin's lymphoma, acute renal failure (ARF) was the most commonly observed kidney damage. Varela also found a higher number of patients with CKD among those diagnosed with myeloma.[38]

Corlu and colleagues associated the diagnosis of lymphoma with some degree of renal involvement in 83,5 % of cases, with AKI being the most common. Histologically, interstitial infiltrated was the most common renal lesion (97,1 %).[39] The worsening or exacerbation of CKD has also been associated with a diagnosis of lymphoma.[40]

In a review of the literature, we found more than 150 cases of glomerulonephritis associated with Hodgkin's lymphoma, with only 5 % of these cases being membranous glomerulonephritis.[41]

Renal involvement in hematological neoplasms is common. Acute renal failure occurs in up to 60 % of patients, and the etiology is varied. On the other hand, the development of chronic kidney disease (CKD) is multifactorial and determines the prognosis of the disease. In addition, improved survival with the advent of new cancer therapies increases the prevalence of patients with CKD.[42]

Although the literature reports acute renal failure (ARF) as the most common renal damage in patients with oncohematological diseases, the predominance in this study of patients with acute chronic kidney disease (CKD) could be due to the fact that in the Cuban population over 60 years of age, which was predominant in the study, there is a high incidence of chronic non-communicable diseases,[43] which in the long term impair renal function, with an increase in the number of patients with chronic kidney disease (CKD),[44] which is also screened for in primary health care with glomerular filtration studies, thus ensuring diagnosis in the early stages, which could mean that CKD is diagnosed before the neoplastic disease.

Kidney damage in hematological neoplasms may be due to the neoplasm itself or to cancer treatments, and the lesions can affect any part of the kidney. The etiology of kidney damage secondary to the neoplasm itself is diverse and can be classified according to the segment of the nephron affected:[45]

Vascular lesions: due to vascular occlusion caused by disseminated intravascular coagulation or hyperleukocytosis, or renal vein thrombosis.

- Glomerular lesions: the glomerulus may be affected by the appearance of various forms of glomerulonephritis, such as minimal change glomerulonephritis (more common in LH), focal segmental glomerulosclerosis, or membranoproliferative glomerulonephritis.
- Proximal tubule lesions: acute tubular necrosis, lysozymuria, hypercalcemia and nephrocalcinosis, or Fanconi syndrome are very common.
- Tubulointerstitial lesions: common in interstitial lymphoid infiltration, radiation nephropathy, and hemophagocytic lymphohistiocytosis with acute interstitial damage.
- Lesions in the collecting tubules: as in tubular obstruction by paraproteins, such as in multiple myeloma, in uric acid nephropathy (usually associated with tumor lysis syndrome), or in BK virus nephropathy.
- Obstructive uropathy due to retroperitoneal adenopathies.

In addition, these patients are at risk for ARF, such as volume depletion, sepsis, and other comorbidities, especially in elderly patients, such as hypertension, diabetes mellitus, congestive heart failure, etc.[42]

Among the above causes, renal infiltration by neoplastic cells is common in hematological neoplasms, and

the clinical presentation can range from asymptomatic to ARF. ARF due to renal infiltration occurs in only 1 % of acute leukemias and <1 % of lymphomas or chronic leukemias.[46]

Another form of renal damage in these conditions is the appearance of lysozymuria, or the presence of lysozyme in urine, which can be observed in hematological neoplasms and carcinomatosis. Under normal conditions, lysozyme is filtered by the glomerulus and reabsorbed in the proximal tubule. In some neoplasms, there may be a massive release of lysozyme from neoplastic cells into the blood, exceeding the reabsorptive capacity of the proximal tubule and therefore causing lysozyme to appear in urine, which can cause tubular damage or lysozyme amyloidosis.[47]

Of particular interest is contrast-induced kidney damage in cancer patients. These patients often undergo tests that require the use of iodinated contrast agents to monitor the progression of their disease.[48] The cumulative dose of iodinated contrast with repeated procedures increases the risk of kidney injury and reduces survival. In fact, the KDIGO guidelines consider the specific case of cancer patients, recommending delaying further exposure in cases of kidney injury.[49]

In addition to the relationship between oncohematological diseases and existing kidney damage at diagnosis, the association between these diseases and the need for hemodialysis was studied, and the results are shown in figure 4.

| Enfermedad oncohematológica | Necesidad de Hemodiálisis | | | | | | $X^2$ | P |
|---|---|---|---|---|---|---|---|---|
| | Sí | | No | | Total | | | |
| | No. | % | No. | % | No. | % | | |
| Mieloma múltiple | 8 | 15.1 | 16 | 30.2 | 24 | 45.3 | 4.22 | 0.04* |
| Linfoma no Hodgking | 3 | 5.7 | 10 | 18.9 | 13 | 24.5 | 0.05 | 0.81 |
| Leucemia linfoide crónica | 0 | 0 | 4 | 7.5 | 4 | 7.5 | 1.13 | 0.28 |
| Leucemia mieloide crónica | 0 | 0 | 8 | 15.1 | 8 | 15.1 | 2.46 | 0.12 |
| Linfoma Hodgking | 0 | 0 | 4 | 7.5 | 4 | 7.5 | 1.13 | 0.28 |
| Total | 11 | 20.8 | 42 | 79.2 | 53 | 100 | - | - |

**Figure 4.** Association between oncohematological diseases and the need for hemodialysis

The study found that 20,8 % of patients were on hemodialysis, with these patients diagnosed with multiple myeloma and non-Hodgkin's lymphoma. When analyzing the relationship between diagnosis and the need for hemodialysis, it was found that the need for hemodialysis to treat this type of patient was significantly associated with a diagnosis of multiple myeloma with 95 % certainty.

Due to the high frequency of kidney damage with acute kidney injury (AKI), chronic kidney disease (CKD), or worsening of existing CKD in patients with multiple myeloma, researchers have linked this disease to the need for hemodialysis in most patients.[50]

In a population study conducted in 2019 in Tunisia, Africa, on 1,038 patients with newly diagnosed myeloma, 25 % had some degree of renal failure and 13 % required dialysis. It has been shown that in addition to the immediate use of anti-myeloma agents to reduce the production of free light chains in serum, their high concentrations can be reduced by extracorporeal techniques.[51] Other authors agree on the need for hemodialysis in these patients as important for the recovery of renal function.[52]

| Medicamentos | Necesidad de Hemodiálisis | | | | | | $X^2$ | p | OR | Intervalo de confianza | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Sí | | No | | Total | | | | | | |
| | No. | % | No. | % | No. | % | | | | Li | Ls |
| Dexametasona | 5 | 9.4 | 9 | 17.0 | 14 | 26.4 | 2.58 | 0.11 | 3.05 | 0.75 | 12.35 |
| Prednisona | 3 | 5.7 | 19 | 35.8 | 22 | 41.5 | 1.15 | 0.28 | 0.45 | 0.11 | 1.95 |
| Vincristina | 2 | 3.8 | 18 | 34.0 | 20 | 37.7 | 2.25 | 0.13 | 0.29 | 0.06 | 1.54 |
| Adriamicina | 2 | 3.8 | 11 | 20.8 | 13 | 24.5 | 0.30 | 0.58 | 0.63 | 0.12 | 3.36 |
| Citisor | 2 | 3.8 | 6 | 11.3 | 8 | 15.1 | 0.11 | 0.75 | 1.33 | 0.23 | 7.74 |
| Cisplatino | 2 | 3.8 | 4 | 7.5 | 6 | 11.3 | 0.65 | 0.42 | 2.11 | 0.33 | 13.37 |
| Etopósido | 2 | 3.8 | 1 | 1.9 | 3 | 5.7 | 4.08 | 0.04* | 9.11 | 1.74 | 111.72 |
| Ciclofosfamida | 1 | 1.9 | 13 | 24.5 | 14 | 26.4 | 2.14 | 0.14 | 0.22 | 0.03 | 1.93 |
| Talidomida | 1 | 1.9 | 2 | 3.8 | 3 | 5.7 | 0.30 | 0.58 | 2.00 | 0.16 | 24.32 |
| Hidroxiurea | 0 | 0 | 2 | 3.8 | 2 | 3.8 | 0.54 | 0.46 | 0.78 | 0.67 | 0.91 |
| Bleomicina | 0 | 0 | 2 | 3.8 | 2 | 3.8 | 0.54 | 0.46 | 0.78 | 0.67 | 0.91 |
| Ac Soledronio | 0 | 0 | 1 | 1.9 | 1 | 1.9 | 0.26 | 0.61 | 0.78 | 0.68 | 0.91 |

**Figure 5**. Association between drugs used in the treatment of patients and the need for hemodialysis

There is growing evidence from large observational registries that have consistently shown that the risk

of cancer increases at least 2- to 3-fold in patients on dialysis with mild or moderate CKD. The interactions between cancer and CKD have posed significant challenges in the management of these patients.[32]

Another factor that may have influenced the need for hemodialysis as a treatment for kidney damage is the drugs used to treat oncohematological diseases. The results are shown in figure 5.

Among the drugs used in oncohematological therapy, the most commonly used was prednisone (41,5 %), followed by vincristine (37,7 %), which was also associated with the need for hemodialysis. The use of Etoposide was found to be significantly associated with the need for hemodialysis. Furthermore, it was found that the use of this drug increases the likelihood of needing hemodialysis in oncohematological patients by nine times.

In patients with oncohematological diseases, the use of conventional chemotherapy and innovative treatments is necessary: targeted agents against growth factors and their receptors, antiangiogenic drugs, immunoregulatory proteins, cell cycle regulators or enzyme blockers, and others. All these treatments will improve outcomes for cancer and hematological diseases, but they are not without secondary problems affecting the kidneys.[24]

Among the drugs used in oncohematological therapy in these patients, the most widely used was prednisone, followed by vincristine, which did not show a significant relationship with the need for hemodialysis. The use of etoposide was found to be significantly associated with the need for hemodialysis. In addition, it was found that the use of this drug increases the likelihood of needing hemodialysis in oncohematological patients by nine times.

Kidney damage secondary to treatment in patients with hematological neoplasms is very common. Classic chemotherapy agents are associated with varying degrees of toxicity, and kidney toxicity is common. However, new therapeutic agents, although less toxic, have also been associated with multiple renal alterations, which have been described in recent years. This supports the results obtained, where chemotherapy agents were associated with the need for hemodialysis, but only in one case was this association significant.

The etiology of treatment-related kidney damage is diverse and can be classified according to the segment of the nephron affected. Broadly speaking, some have been linked to vascular lesions of thrombotic microangiopathy or glomerular lesions, and others to the development of tubulointerstitial nephritis.[45]

Etoposide was the drug most closely associated with the need for hemodialysis. This drug is a semisynthetic podophyllin used in cancer treatment. Its mechanism of action is to inhibit the multiplication of tumor cells. Its half-life is 6-8 hours in patients with normal renal function, but it is prolonged in renal failure. Consequently, dose adjustment is required in renal failure based on creatinine clearance. This drug alone is not capable of causing kidney damage, so in the patients studied, it is more related to their advanced age and association with other diseases, particularly a history of chronic kidney disease.[53]

For all the above reasons, it was necessary to analyze the evolution of these patients, and the results are shown in figures 6 and 7.

| Progreso | Enfermedad renal inicial | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | ERC | | ERC agudizada | | IRA | | Total | |
| | No. | % | No. | % | No. | % | No. | % |
| ERC | 12 | 22.6 | 11 | 20.8 | 7 | 13.2 | 30 | 56.6 |
| Estadio 3a | 2 | 6.7* | 1 | 3.3* | 2 | 6.7* | 5 | 16.7* |
| Estadio 3b | 4 | 13.3* | 4 | 13.3* | 3 | 10.0* | 11 | 36.7* |
| Estadio 4 | 6 | 20.0* | 5 | 16.7* | 2 | 6.7* | 13 | 43.3* |
| Estadio 5 | 0 | 0.0* | 1 | 3.3* | 0 | 0.0* | 1 | 3.3* |
| Fallecido | 1 | 1.9 | 10 | 18.9 | 3 | 5.7 | 14 | 26.4 |
| IRA recuperada | 0 | 0.0 | 0 | 0.0 | 9 | 17.0 | 9 | 17.0 |

**Figure 6**. Progression of initial kidney disease

When analyzing the evolution of the patients, it was observed that 56,6 % progressed to different stages of chronic kidney disease (CKD), 7 of whom were patients who started with acute renal failure (ARF) and then progressed to stages 3 and 4 of chronicity. Only one patient who initially presented with acute chronic kidney disease (CKD) progressed to stage 5 CKD. Seventeen percent of all patients recovered from acute renal failure (ARF), and 26,4 % died. Ten of the 14 patients who died began with acute chronic kidney disease (CKD) (18,9 % of all patients).

When analyzing the evolution of the patients, it was observed that 56,6 % progressed to different stages of CKD, 7 of whom were patients who began with AKI and then progressed to stages 3 and 4 of chronicity. Seventeen percent of all patients recovered from ARF and 26,4 % died. Ten patients out of a total of 14 who died began with acute kidney disease and the disease that caused a significantly higher number of deaths was multiple myeloma, with a 13-fold increased risk of death from kidney disease.

The proven relationship between oncohematological diseases and renal failure, especially multiple myeloma, already documented, supports the results obtained, where a low percentage of patients with ARF recovered

and the rest, together with those who already had CKD, progressed to stages 3 and 4 of the disease. However, only one patient progressed to stage 5, which shows good results in cancer treatment and hemodialysis. The higher incidence of multiple myeloma in the sample and the impact of this disease on renal function justify the higher mortality in these patients.

This last result made it necessary to look for an association between lethal progression and oncohematological disease.

| Enfermedad oncohematológica | Fallecido | | | | | | $X^2$ | p | OR | Intervalo de confianza | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Sí | | No | | Total | | | | | | |
| | No. | % | No. | % | No. | % | | | | Li | Ls |
| Mieloma múltiple | 12 | 22.6 | 12 | 22.6 | 24 | 45.3 | 12.55 | 0.00* | 13.50 | 2.61 | 69.88 |
| Leucemia mieloide crónica | 1 | 1.9 | 7 | 13.2 | 8 | 15.1 | 0.93 | 0.33 | 0.35 | 0.04 | 3.15 |
| Linfoma no Hodgking | 1 | 1.9 | 12 | 22.6 | 13 | 24.5 | 3.10 | 0.08 | 1.73 | 0.02 | 1.47 |
| Linfoma Hodgking | 0 | 0.0 | 4 | 7.5 | 4 | 7.5 | 1.55 | 0.21 | 0.71 | 0.59 | 0.85 |
| Leucemia linfoide crónica | 0 | 0.0 | 4 | 7.5 | 4 | 7.5 | 1.55 | 0.21 | 0.71 | 0.59 | 0.85 |
| Total | 14 | 26.4 | 39 | 73.6 | 53 | 100.0 | | | | | |

**Figure 7**. Association between progression to death and the oncohematological disease causing kidney disease

Figure 7 shows that the disease that caused a significantly higher number of deaths among the patients studied was multiple myeloma with 95 % certainty. It was also found that patients diagnosed with multiple myeloma who have kidney damage are 13 times more likely to die from kidney disease. There were no deaths among cases with Hodgkin's lymphoma and chronic lymphocytic leukemia.

In a study consulted, the median survival was only 21 months in patients with renal failure, and among the factors associated with overall survival at 1 year were a diagnosis of myeloma and response in terms of improved renal function. Twenty-one patients died.[51] These results are consistent with the present study.

Although survival of MM patients on dialysis remains low, a significant proportion survive more than three years, and there is also evidence of a trend toward longer survival in the last decade.[38] Other authors report high survival in patients with this disease undergoing renal replacement therapy.[54]

## CONCLUSIONS

- Among oncohematological patients with kidney disease, males, ages 58 to 67, and Caucasians predominate.
- The most commonly observed oncohematological disease is multiple myeloma, and the most frequent kidney disease is CKD.
- Multiple myeloma and the use of etoposide are associated with the need for hemodialysis.
- Most patients progressed to different stages of chronic kidney disease.
- Multiple myeloma is significantly associated with death.

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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