

Original Article

Renal Impairment at Multiple Myeloma Diagnosis: Clinical Characteristics, Contributing Factors in a Retrospective Cohort

Authors & 

¹Eda Çeker, ²Zübeyde Nur Özkurt, ²Zeynep Arzu Yeğin, ²Galip Güz, ²Rauf Haznedar

¹Etilik City Hospital, Department of Internal Medicine, Ankara, Türkiye, ²Gazi University, Department of Internal Medicine, Ankara, Türkiye

Corresponding: Eda Çeker, M.D., Ankara Etilik City Hospital, Department of Internal Medicine, Ankara, Türkiye. **E-mail:** edapkr@

DOI: [10.5281/zenodo.1844521](https://doi.org/10.5281/zenodo.1844521)

All articles are published under the Creative Commons Attribution 4.0 International (CC BY 4.0) license. For further details and updates, www.jeimp.com, www.hdtv.info, and www.digitalmkd.com

Abstract

Background: This study aimed to examine the frequency and clinical characteristics of kidney dysfunction at the time of multiple myeloma (MM) diagnosis, focusing on factors associated with MM-related nephropathy, to identify factors associated with renal recovery among patients presenting with impaired kidney function.

Methods: This retrospective single-center study included patients diagnosed with MM between 1999 and 2009. Of 204 screened patients, 136 were eligible for analysis after exclusion of cases with incomplete laboratory or imaging data. Kidney dysfunction was defined as estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m² at diagnosis. Demographic characteristics, myeloma subtype, International Staging System (ISS) stage and risk category, laboratory parameters, renal ultrasonography findings, and nephrotoxic exposures were evaluated. Renal recovery was assessed in patients with kidney dysfunction at baseline.

Results: Kidney dysfunction was present in 24 patients (17.6%) at diagnosis. Compared with those with preserved renal function, these patients had higher rates of light chain myeloma, and higher β2-microglobulin and CRP levels, and greater proteinuria (all $p \leq 0.05$). Moreover, patients with kidney dysfunction were more likely to have higher ISS Stage, high-risk ISS classification ($p < 0.001$). Renal ultrasonography abnormalities including increased cortical echogenicity and reduced kidney size, were significantly more common in the kidney dysfunction group ($p < 0.001$). Among patients with kidney dysfunction, renal recovery occurred in 9 of 24 (37.5%). Lower baseline creatinine and absence of hemodialysis requirement at diagnosis were associated with higher recovery likelihood, whereas increased cortical echogenicity or reduced kidney size predicted persistent dysfunction.

Conclusion: Kidney dysfunction at diagnosis in MM patients is associated with advanced disease stage, and unfavorable laboratory and clinical features. While β2-microglobulin remains a useful prognostic marker, its interpretation in patients with kidney dysfunction should be approached cautiously due to impaired renal clearance. These findings underscore the importance of early recognition and appropriate management of renal impairment in MM.

Keywords: Multiple Myeloma, Renal Insufficiency, Myeloma Kidney, Recovery of Function

Submitted at: 07.01.2026, **Accepted at:** 28.01.2026, **Published at:** 01.01.2026

INTRODUCTION

Multiple myeloma (MM) is a malignant plasma cell disorder characterized by clonal proliferation of plasma cells in the bone marrow and the presence of monoclonal immunoglobulins or light chains. Clinically, MM presents with lytic bone lesions, anemia, hypercalcemia, renal dysfunction, and recurrent infections. Following non-Hodgkin lymphoma, it is the second most common hematologic malignancy in adults, typically diagnosed between 60 and 70 years of age (1,2). Globally, MM affects approximately 35,000 individuals annually in the United States and nearly 600,000 worldwide per year (3).

Renal impairment is one of the clinically important complications of MM (4). Renal impairment is observed in approximately 20–40% of patients at diagnosis, and up to 50–75% may experience renal involvement at some point during the disease course (4–6). Kidney involvement in MM may occur either through direct monoclonal light chain-mediated tubular injury or secondary mechanisms such as dehydration, hypercalcemia, infections, nephrotoxic medications, and other comorbid conditions (4,7). Such renal complications substantially worsen the clinical trajectory, as renal failure (RF) ranked as the second most frequent cause of mortality among MM patients (surpassed only by infections) particularly

before widespread access to dialysis became available (4,7).

Lambda and kappa light chains are the two main types of free light chains. Lambda light chains are more frequently associated with severe tubular injury and more aggressive renal involvement, leading to faster progression of renal dysfunction compared with kappa light chains. These pathological changes result from the deposition of monoclonal light chains within the renal tissue, which can give rise to cast nephropathy, light chain deposition disease, or AL amyloidosis (8,9). Chronic structural changes such as increased cortical echogenicity or reduced kidney size, may also develop over time as a result of sustained tubular injury and interstitial fibrosis in MM-related renal involvement (10). Renal failure has been a major contributor to mortality in MM, accounting for a substantial proportion of deaths in historical cohorts. A 12-month follow-up analysis showed that reversibility of renal failure was a more important prognostic factor than chemotherapy response (11,12).

Given the substantial clinical impact of renal involvement in MM, this study therefore aimed to evaluate the clinical characteristics, laboratory features, and disease severity associated with kidney dysfunction at the time of MM diagnosis. The secondary aim was to describe comorbid factors and nephrotoxic exposures that may contribute to impaired renal function in this cohort.

METHODS

Protocol and Search Strategy

This retrospective single-center study was conducted at Gazi University Faculty of Medicine, Department of Internal Medicine, hematology and nephrology divisions, using data from adult patients diagnosed with MM between January 1, 1999, and December 31, 2009. Ethical approval was obtained from the Ankara Keçiören Training and Research Hospital, The Committee of Human Researches, dated 25.11.2009 and numbered 2009/11-110. The study involved analyzing retrospective data, and no budget was required.

Case selection: \geq 18-year-old adult patients with MM. Patients diagnosed at Gazi University School of Medicine, Department of Internal Medicine were included in the study.

Staging and Risk stratification for MM: International Staging System (ISS) for Multiple Myeloma was utilized for staging (Accessed at: 24.06.2024, <https://www.myeloma.org/international-staging-system-revised-iss-r-iss>) (13).

Definition of Kidney Dysfunction: Kidney dysfunction was defined primarily by eGFR <60 mL/min/1.73 m² at

diagnosis. Among patients with eGFR <60 mL/min/1.73 m² at diagnosis, four individuals with clearly documented long-standing chronic kidney disease (persistently reduced eGFR for >1 year prior to MM diagnosis) were excluded from the renal dysfunction group in statistical analyses, in order to focus on kidney impairment present at or newly recognized at MM diagnosis. This exclusion was intended to minimize confounding by pre-existing CKD and to better capture kidney impairment present at or newly recognized at MM diagnosis, which is more likely to reflect MM-related renal involvement. Creatinine clearance and 24-hour proteinuria levels were used to further stage CKD, in accordance with KDIGO principles (14).

Exclusion criteria: Monoclonal gammopathy of undetermined significance, Waldenström macroglobulinemia, incomplete patient data, and an external diagnosis of MM were considered for exclusion. Data collection: Demographical features of the patients, stage of the disease, comorbidities, nephrotoxic drug, and radiocontrast agent use were noted. The treatment protocols and responses to the treatment and ISS stage and ISS risk category were also noted. Ig G, A, and M levels measured at the time of diagnosis, serum protein, albumin, globulin, β 2 microglobulin, hemoglobin (Hgb), white blood cell (WBC), platelet (PLT), erythrocyte sedimentation rate (ESR), C-reactive protein [CRP]), blood urea nitrogen (BUN), creatinine, uric acid, calcium, LDH, 24-h creatinine clearance (Ccr) and 24-h proteinuria, and plasma cell ratio in bone marrow biopsy (BMR) and abdominal ultrasonography are evaluated. Serum free light chain (FLC) data were available only in a subset of patients (125/136) and were analyzed where recorded. If renal ultrasonography was performed (clinical indication/physician's discretion), it was recorded and was available for 90 patients.

Primary outcomes: The primary objectives of this study were to determine the frequency of kidney dysfunction at the time of MM diagnosis and to characterize its associated clinical, laboratory, and disease-related features. In patients presenting with kidney dysfunction, an additional primary aim was to identify factors associated with renal recovery during follow-up, including biochemical markers, clinical variables, and structural renal findings on ultrasonography. These outcomes were selected to better define the early renal involvement profile of newly diagnosed MM and to clarify prognostic indicators of renal reversibility within this cohort.

Secondary outcomes: Secondary outcomes included describing the demographic, clinical, and laboratory characteristics of the overall MM cohort and examining the distribution of myeloma subtypes, ISS stage, ISS risk

Table 1. Baseline Demographic and Clinical Characteristics of the Participants

Characteristic	Category	n (%)
Gender	Male	72 (52.9)
	Female	64 (47.1)
Age (years)		62 (38–90)
Myeloma Type	IgG	85 (62.5)
	IgA	22 (16.3)
	IgD	4 (2.9)
	IgM	1 (0.7)
	Kappa light chain	11 (8.1)
	Lambda light chain	11 (8.1)
	Non-secretory	2 (1.5)
ISS Stage*	Stage I	30 (24.2)
	Stage II	38 (30.6)
	Stage III	56 (45.2)
ISS Risk Category †	Low risk	25 (22.9)
	Intermediate risk	45 (41.3)
	High risk	39 (35.8)
Renal Function at Diagnosis	No kidney dysfunction	112 (82.4)
	Kidney dysfunction	24 (17.6)

ISS, International Staging System.

categories, and renal ultrasound findings. Additional analyses also explored the frequency of nephrotoxic exposures and comorbid risk factors at diagnosis, providing a broader clinical context for understanding kidney involvement in MM.

Treatment protocols and Responders: Only the induction treatment was noted and its impact on outcomes was assessed. Response to treatment was assessed in patients who received at least two cycles of chemotherapy. Patients with partial or complete responses were considered responders. Patients who died within the first two months, who gave up the center's follow-up schedule, and who did not complete yet two cycles of chemotherapy during data acquisition, were not included in the statistical analysis.

Serum immunoglobulin measurement, monoclonal protein detection: Freelite nephelometry method and BNII nephelometer were used to measure serum immunoglobulin levels. Dade Behring kits were used to measure serum Ig levels. The presence and types of monoclonal proteins were studied in the Gazi University Faculty of Medicine Adult Hematology Laboratory. Serum samples were studied with the IFE method on the Beckman device and the resulting bands were evaluated.

STATISTICAL ANALYSIS

IBM SPSS 11.5 (Chicago, IL, USA) statistical software was utilized for analyzing the data collected. The Kolmogorov-Smirnov test was employed to determine whether the numerical variables have a normal distribution. Descriptive statistics were presented as

mean \pm standard deviation (SD) or median (minimum–maximum) and as the number of cases and (%) for categorical variables. Chi-square was employed to assess categorical variables. Independent Samples t-test or Mann-Whitney U test was used for evaluating continuous variables. Independent risk factors were evaluated using univariate analyses; Multivariable regression was not performed due to the limited number of renal recovery events. Such models would carry a high risk of overfitting and unstable estimates. Statistical significance was defined as $p < 0.05$.

RESULTS

A total of 136 patients diagnosed with multiple myeloma (MM) between 1999 and 2009 were included in the analysis. The cohort consisted of 72 men (52.9%) and 64 women (47.1%), with a median age of 62 years (38–90). At diagnosis, 112 patients (82.4%) had intact immunoglobulin myeloma, 22 (16.2%) had light chain myeloma and 2 (1.5%) had non-secretory disease. Among intact immunoglobulin types, IgG was the most frequent (62.5%), followed by IgA (16.3%), IgD (2.9%), and IgM (0.7%). Kappa and lambda light chain myeloma were each observed in 11 patients (8.1%) (**Table 1**). According to the ISS, 24.2% of patients were Stage I, 30.6% Stage II, and 45.2% Stage III. The median follow-up was 14.5 months (1–127).

Kidney dysfunction (eGFR <60 mL/min/1.73 m 2) was present in 24 patients (17.6%) at diagnosis. Nephrotic-range proteinuria (≥ 3500 mg/day) was present in 23 patients (16.9%), whereas 52 (38.2%) had proteinuria between 300 and 3500 mg/day and 61 (44.9%) had

Table 2. Comparison of Clinical and Laboratory Features Between Patients With and Without Kidney Dysfunction

Feature	Kidney Dysfunction (n = 24)	No Kidney Dysfunction (n = 112)	p-value
Gender , % (n)			
Male	75.0 (18)	48.2 (54)	
Female	25.0 (6)	51.8 (58)	0.02
Age, years (mean ± SD)	60.0 ± 9.7	63.0 ± 10.2	0.250
Myeloma type			
– Intact immunoglobulin	16 (66.7%)	96 (85.7%)	0.002
– Light chain	7 (29.2%)	15 (13.4%)	
– Non-secretory	1 (4.2%)	1 (0.9%)	
Monoclonal antibody type			
– IgG	10 (41.6%)	75 (66.9%)	0.312
– IgA	4 (16.7%)	18 (16.0%)	
– IgD	2 (8.3%)	2 (1.8%)	
Light chain type			
– Kappa	11 (45.8%)	59 (52.7%)	0.456
– Lambda	12 (50.0%)	52 (46.2%)	
Free Light Chain (n=125)	21.4 (146)	30.4 (160)	0.967
– Kappa (n=64)	15 (234.8)	376.5 (4967.6)	0.002
– Lambda(n=61)			
ISS Stage			
– Stage I	0 (0%)	30 (29.1%)	<0.001
– Stage II	1 (4.7%)	37 (35.9%)	
– Stage III	20 (95.3%)	36 (34.9%)	
ISS Risk Category			
– Low	1 (5.5%)	24 (26.4%)	<0.001
– Intermediate	3 (16.7%)	42 (46.2%)	
– High	14 (77.8%)	25 (27.5%)	
Hemoglobin, g/dL	9.7 ± 2.1	9.9 ± 2.3	0.328
WBC (/mm ³)	7326 ± 2820	6024 ± 2141	0.010
Platelets (×10 ³ /mm ³)	204 ± 95	232 ± 88	0.460
Creatinine, mg/dL	3.99 ± 1.71	1.06 ± 0.32	<0.001
Calcium, mg/dL	9.6 ± 2.1	9.6 ± 1.6	0.856
Phosphorus, mg/dL	4.8 ± 2.1	3.8 ± 3.0	0.050
Uric acid, mg/dL	7.8 ± 2.0	6.1 ± 2.4	0.004
β2-microglobulin, mg/L	296.15 ± 191.25	126.35 ± 105.20	<0.001
24-h urine protein (mg/day)	490.20 ± 267.10	169.59 ± 133.02	<0.001
CRP (mg/dL)	35.12 ± 26.10	18.38 ± 12.60	0.020
Other renal risk factors			
– NSAID use	8 (33.3%)	15 (13.4%)	0.030
– Hyperuricemia	12 (54.5%)	30 (29.1%)	0.020
– Contrast exposure	7 (29.2%)	18 (16.1%)	0.040
Ultrasound findings			
– Normal	8 (40.0%)	59 (84.3%)	<0.001
– Increased echogenicity	8 (40.0%)	5 (7.1%)	
– Small kidneys	4 (20.0%)	3 (4.3%)	

β2-microglobulin: Beta-2 microglobulin; CRP: C-reactive protein; NSAID: Non-steroidal Anti-inflammatory Drug

<300 mg/day. Among patients with kidney dysfunction at diagnosis, 9 (6.6% of the total cohort) required hemodialysis (HD). One of these patients could be weaned from HD within one month of follow-up.

When patients with and without kidney dysfunction were compared, age did not differ significantly, but kidney dysfunction was more common in men (75.0% vs. 48.2%; p = 0.02) (**Table 2**). Light chain myeloma was more frequent in those with kidney dysfunction (29.2% vs. 13.4%; p = 0.02), while intact immunoglobulin

types and light chain isotypes showed no meaningful differences (**Figure 1**). Serum FLC data were available in 125 patients; free lambda levels were significantly higher in the kidney dysfunction group, whereas free kappa levels did not differ between groups. Disease severity was strongly associated with renal status: 95.3% of patients with kidney dysfunction were ISS Stage III compared with 34.9% of those with preserved kidney function, and 77.8% were classified as high risk (both p < 0.001) (**Figure 2**).

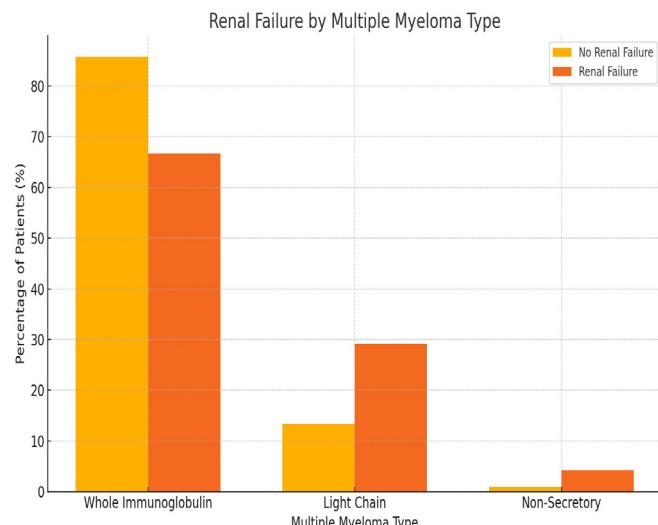


Figure 1. Free light chain in multiple myeloma poses higher risk of kidney disease

Laboratory markers of renal impairment including phosphorus and 24-hour proteinuria were significantly worse in patients with kidney dysfunction, and inflammatory markers (β 2-microglobulin, CRP, WBC) were also higher (all $p \leq 0.05$). Additional renal risk factors showed significant differences for hyperuricemia (54.5% vs. 29.1%; $p = 0.02$), NSAID use (33.3% vs. 13.4%; $p = 0.03$), and radiocontrast exposure (29.2% vs. 16.1%; $p = 0.04$) (Table 2). Other factors—including sepsis, hypercalcemia, hypertension, type II diabetes mellitus, and heart failure—were not significantly different between the groups, although several were numerically more frequent in patients with kidney dysfunction.

Renal ultrasonography (performed in 90 patients) showed abnormal findings more frequently in the kidney dysfunction group ($p < 0.001$). Among those without kidney dysfunction, 59 (84.3%) had normal renal findings, 5 (7.1%) increased echogenicity, 3 (4.3%) enlarged kidneys, and 3 (4.3%) reduced kidney size. In contrast, among patients with kidney dysfunction, only 8 (40.0%) had normal USG findings, whereas 8 (40.0%) showed increased echogenicity and 4 (20.0%) had reduced kidney size.

Although the number of patients with kidney dysfunction

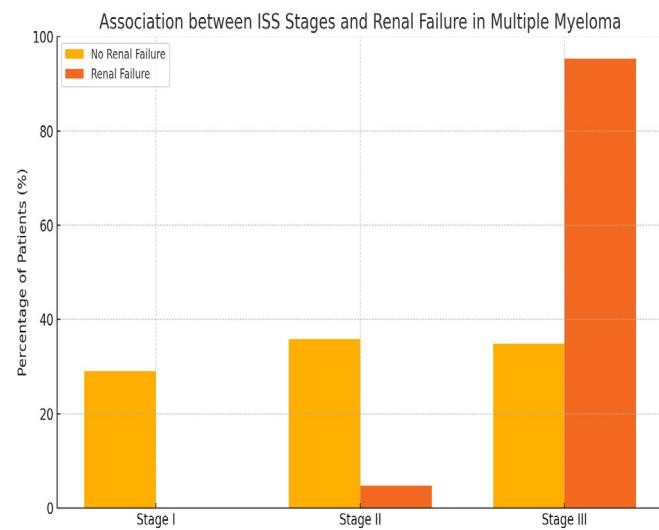


Figure 2. The frequency of kidney disease increase with advance in ISS stages

was limited, renal recovery outcomes were evaluated using the available data. Among the 24 patients with kidney dysfunction, renal recovery was achieved in 9 (37.5%). The median recovery time was 1 month (0.5–10 months). Lower baseline creatinine favored recovery (3.24 ± 1.8 vs. 4.45 ± 1.5 mg/dL; $p = 0.05$), and the need for hemodialysis at presentation markedly reduced the likelihood of improvement (53.3% vs. 11.1%; $p = 0.03$). Renal USG findings were associated with recovery, whereas increased echogenicity or reduced kidney size predicted persistent dysfunction ($p = 0.009$) (Table 3). Other variables, including diabetes mellitus, heart failure, proteinuria level, NSAID use, MM subtype, light chain type, ISS stage and risk category, and response to induction chemotherapy, were also examined but showed no statistically significant association with renal recovery. These factors were analyzed in the full dataset, and showed no meaningful clinical trend and were therefore not included in the summary table, which lists only statistically significant or clinically relevant predictors.

DISCUSSION

Renal impairment is a well-recognized and clinically relevant complication of multiple myeloma (MM), with

Table 3. Key Factors Associated With Renal Recovery in Patients With Kidney Dysfunction

Factor	Recovered n (%)	Not Recovered n (%)	P value
Hemodialysis at diagnosis†	1 (11.1)	8 (88.9)	0.03
Baseline creatinine >4 mg/dL†	1 (10.0)	9 (90.0)	0.02
Renal USG findings			
– Normal	5 (62.5)	3 (37.5)	0.009
– Increased echogenicity	0 (0)	8 (100)	0.009
Hypertension	3 (21.4)	11 (78.6)	0.05

important implications for prognosis, treatment response and survival outcomes (4,7). This study investigates the outcomes, risk factors, and clinical characteristics of renal dysfunction in a cohort of 136 MM patients.

Although MM is reported to be more frequent in males, and worse outcomes in females, the underlying reasons are not well understood 15,16. This cohort showed a higher number of male patients (52.9%), but this sex difference was not statistically significant. However, male predominance within the renal dysfunction subgroup was notable and statistically significant (75% vs. 48.2%, $p=0.002$), aligning with previous epidemiologic data suggesting greater susceptibility to renal complications among male MM patients 15,16. Age did not differ significantly between patients with and without kidney dysfunction (60.0 ± 9.7 vs. 63.0 ± 10.2 years; $p > 0.05$) in our cohort, contrary to some population-based studies that have identified advanced age as a risk factor for renal involvement in MM (5,6).

Other comorbidities such as sepsis, hypercalcemia, diabetes mellitus, hypertension, and heart failure, were more common numerically among patients with renal dysfunction but did not reach statistical significance. Prior research has linked several of these factors (particularly hypercalcemia, sepsis, and cardiovascular comorbidities) to worsening renal function in MM (17). The absence of statistical significance in our analysis may reflect the limited sample size of the renal dysfunction, which may reduce the power to detect clinically meaningful associations.

Renal dysfunction was detected in 17.6% of patients at diagnosis, consistent with previously reported prevalence rates in newly diagnosed MM populations (5,6). Patients with kidney dysfunction exhibited more advanced disease stages and were predominantly classified as high-risk according to the ISS, reflecting the strong association between tumor burden and renal impairment. Laboratory markers including β 2-microglobulin, and inflammatory markers, were significantly worse in this group, supporting prior evidence that both monoclonal protein-mediated tubular injury and systemic inflammatory activation contribute to early renal compromise in MM (18-20). Also light chain myeloma was more common in patients with kidney dysfunction, consistent with the well-described nephrotoxic potential of circulating free light chains, which exert direct tubular toxicity and promote cast formation (21,22). In parallel with this observation, free light chain profiles demonstrated clear biochemical differences between groups: serum free lambda light chain levels were markedly higher among patients with renal dysfunction, whereas free kappa light chain levels showed no significant difference. This pattern supports

prior evidence indicating that lambda light chains possess greater nephrotoxic potential in MM (22,23). Beyond their mechanical obstructive effects, degraded light chains also trigger a robust inflammatory response within the renal microenvironment. Experimental data have shown that filtered light chains induce production of pro-inflammatory cytokines including MCP-1, IL-6 and IL-8, and catalyze reactive oxygen species generation, leading to leukocyte infiltration, matrix deposition, and tubulointerstitial fibrosis (19,20). These pathological mechanisms may partly contribute to the higher CRP, high-sensitivity CRP, uric acid, and globulin levels observed in the renal dysfunction subgroup of this cohort, suggesting, although not definitively proving, an amplified systemic and renal inflammatory state (17,24). In addition to monoclonal protein-mediated injury, several immunoglobulin-independent contributors such as hyperuricemia, NSAID and renin-angiotensin system inhibitors exposure, dehydration, sepsis, hypercalcemia, and contrast media, are recognized precipitants of renal injury in MM, and our findings similarly identified NSAID use, elevated serum phosphorus, and contrast exposure as more frequent among patients with kidney dysfunction (17).

High β 2-microglobulin reflects not only the underlying tumor burden but also the degree of renal impairment, as it is affected by both the production of monoclonal proteins and reduced renal clearance. In patients with kidney dysfunction, impaired filtration leads to accumulation of β 2-microglobulin independent of disease activity, thereby diminishing its prognostic specificity in this subgroup (25,26). The association between elevated β 2-microglobulin levels, advanced ISS stages, and renal dysfunction observed in this study is consistent with previous evidence showing that this biomarker is influenced by both tumor mass and renal clearance capacity (25,26).

Renal ultrasonography is a widely used tool in the evaluation of renal impairment. Increased cortical echogenicity and cortical thinning are well-established markers of chronic tubulointerstitial injury and correlate more strongly with adverse histopathologic findings than renal size, parenchymal thickness, or serum creatinine levels (27,28). In our study, patients with kidney dysfunction exhibited markedly higher rates of increased echogenicity and reduced kidney size (features associated with chronic, often irreversible damage) whereas 84.3% of patients without kidney dysfunction showed normal USG findings (19,29). Although conventional B-mode ultrasonography may appear normal in early renal parenchymal disease, the high proportion of normal ultrasonography in patients without renal dysfunction and the clear separation

between groups support the clinical relevance of these findings (30).

Renal recovery was achieved in more than one-third of affected patients. Baseline creatinine levels and need for hemodialysis at diagnosis were strongly associated with recovery outcomes, consistent with prior studies showing that early, aggressive control of free light chain burden is crucial for renal reversibility (10,31,32). Additionally, consistent with the literature, no improvement was observed in any of those with increased cortical echogenicity (29). This reinforces the value of renal ultrasound as a complementary tool in assessing chronicity and reversibility of renal injury in MM. However, given the retrospective nature of the dataset and the older treatment protocols used during 1999–2009, the results should be interpreted with caution. Renal recovery rates in contemporary cohorts may be higher due to earlier diagnosis and the widespread use of bortezomib-based and other novel-agent regimens that rapidly reduce free light chain burden. Therefore, our recovery estimates should be interpreted primarily as reflective of practice patterns in the pre–novel therapy era.

Limitations of the Study

This study has several limitations that should be considered when interpreting the findings. First, retrospective design of the study. Other renal risk factors unrelated to MM were obtained from patients' medical records. Second, because the cohort was treated between 1999 and 2009, the data reflect a pre–novel therapy era. While this limits direct comparability with modern outcomes, the relative homogeneity of treatment practices during this period provides a more uniform clinical context for describing renal involvement at diagnosis. Serum FLC measurements were not available for all patients (available in 125/136 (91.9%)), reflecting limited routine access during the study period. Renal recovery was defined as improvement to eGFR ≥ 60 mL/min/1.73 m², consistent with the conventional threshold separating CKD stage ≥ 3 from preserved renal function. We did not analyze partial recovery separately (i.e., improvement without reaching this threshold), which may underestimate clinically meaningful renal improvement. It should be noted that renal ultrasonography was performed based on clinical indication and physician discretion, and was therefore available only in a subset of patients. This may introduce a degree of selection bias, as patients undergoing ultrasonography were more likely to have suspected or overt renal involvement. Nevertheless, the strong and clinically coherent association observed between ultrasonographic markers of chronicity (particularly increased cortical echogenicity and reduced kidney

size) and lack of renal recovery supports the validity and prognostic relevance of these findings. Moreover, the 10-year duration provides a valuable and uniform clinical perspective on renal dysfunction patterns in MM. Future studies incorporating patients treated with novel agents could offer more contemporary and comprehensive insights into the impact of kidney dysfunction on MM outcomes.

CONCLUSION

The study indicates the significant impact of kidney dysfunction on patients with multiple myeloma, highlighting the importance of early detection and management of renal complications. The findings emphasize the need for regular monitoring of renal function and the cautious use of nephrotoxic agents in MM patients. Future research should focus on elucidating the precise mechanisms driving renal impairment in MM and developing targeted interventions to mitigate these risks. Integrating these insights into clinical practice can potentially improve the prognosis and quality of life for MM patients suffering from renal impairment.

DECLARATIONS

Ethics approval and consent to participate: The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Ankara Keçiören Training and Research Hospital, The Committee of Human Researches, dated 25.11.2009 and numbered 2009/11-110. The study involved analyzing retrospective data, and no budget was required.

Consent for publication: Not applicable

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

Funding: The authors received no specific funding for this study.

AI Assistance: Artificial intelligence–based tools were used in a limited and supportive manner to assist with literature screening, data organization, and language refinement. All study selection, data extraction, statistical analyses, interpretation of results, and final manuscript decisions were performed by the authors. AI tools had no role in study design, outcome definition, data analysis, or clinical interpretation.

REFERENCES

1. National Cancer Institute. Myeloma—Cancer Stat Facts. Surveillance, Epidemiology, and End Results Program. Accessed March 15, 2023. Available from: <https://seer.cancer.gov/statfacts/html/mulmy.html>.
2. Çiftçiler R, Göker H, Demiroğlu H, et al. Evaluation of the survival outcomes of multiple myeloma patients according to their plasmacytoma presentation at diagnosis. *Turk J Haematol.* 2020;37(4):256-262. doi:10.4274/tjh.galenos.2019.2019.0061.

3. Cowan AJ, Green DJ, Kwok M, et al. Diagnosis and management of multiple myeloma: a review. *JAMA*. 2022;327(5):464-477. doi:10.1001/jama.2022.0003.
4. Leung N, Behrens J. Current approach to diagnosis and management of acute renal failure in myeloma patients. *Adv Chronic Kidney Dis*. 2012;19(5):297-302. doi:10.1053/j.ackd.2012.06.001.
5. Augustson BM, Begum G, Dunn JA, et al. Early mortality after diagnosis of multiple myeloma: analysis of patients entered onto the United Kingdom Medical Research Council trials between 1980 and 2002—Medical Research Council Adult Leukaemia Working Party. *J Clin Oncol*. 2005;23(36):9219-9226. doi:10.1200/JCO.2005.03.2086.
6. Dimopoulos MA, Roussou M, Gavriatopoulou M, et al. Bortezomib-based triplets are associated with a high probability of dialysis independence and rapid renal recovery in newly diagnosed myeloma patients with severe renal failure or those requiring dialysis. *Am J Hematol*. 2016;91(5):499-502. doi:10.1002/ajh.24335.
7. Stompor T, Zablocki M, Pankrac K. Renal involvement in multiple myeloma. *Pol Arch Med Wewn*. 2012;122(9):443-448.
8. Basnayake K, Cheung CK, Sheaff M, et al. Differential progression of renal scarring and determinants of late renal recovery in sustained dialysis dependent acute kidney injury secondary to myeloma kidney. *J Clin Pathol*. 2010;63(10):884-887. doi:10.1136/jcp.2010.079236.
9. Kundu S, Jha SB, Rivera AP, et al. Multiple myeloma and renal failure: mechanisms, diagnosis, and management. *Cureus*. 2022;14(2):e22585. doi:10.7759/cureus.22585.
10. Hutchison CA, Cockwell P, Stringer S, et al. Early reduction of serum-free light chains associates with renal recovery in myeloma kidney. *J Am Soc Nephrol*. 2011;22(6):1129-1136. doi:10.1681/ASN.2010080857.
11. Mohty M, Cavo M, Fink L, et al. Understanding mortality in multiple myeloma: findings of a European retrospective chart review. *Eur J Haematol*. 2019;103(2):107-115. doi:10.1111/ejh.13264.
12. Knudsen LM, Hjorth M, Hippe E. Renal failure in multiple myeloma: reversibility and impact on the prognosis. *Eur J Haematol*. 2000;65(3):175-181. doi:10.1034/j.1600-0609.2000.90221.x.
13. International Myeloma Foundation. International Staging System (ISS) and Revised ISS (R-ISS). Accessed April 26, 2024. Available from: <https://www.myeloma.org/international-staging-system-iss-revised-iss-r-iss>.
14. Kidney Disease: Improving Global Outcomes CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl*. 2013;3(1):1-150.
15. Bird S, Cairns D, Menzies T, et al. Sex differences in multiple myeloma biology but not clinical outcomes: results from 3894 patients in the Myeloma XI trial. *Clin Lymphoma Myeloma Leuk*. 2021;21(10):667-675. doi:10.1016/j.clml.2021.04.013.
16. Tsang M, Le M, Ghazawi FM, et al. Multiple myeloma epidemiology and patient geographic distribution in Canada: a population study. *Cancer*. 2019;125(14):2435-2444. doi:10.1002/cncr.32128.
17. Heher EC, Goes NB, Spitzer TR, et al. Kidney disease associated with plasma cell dyscrasias. *Blood*. 2010;116(9):1397-1404. doi:10.1182/blood-2010-03-258608.
18. Heher EC, Rennke HG, Laubach JP, Richardson PG. Kidney disease and multiple myeloma. *Clin J Am Soc Nephrol*. 2013;8(11):2007-2017. doi:10.2215/CJN.12231212.
19. Sengul S, Zwizinski C, Batuman V. Role of MAPK pathways in light chain-induced cytokine production in human proximal tubule cells. *Am J Physiol Renal Physiol*. 2003;284(6):F1245-F1254. doi:10.1152/ajprenal.00350.2002.
20. Wang PX, Sanders PW. Immunoglobulin light chains generate hydrogen peroxide. *J Am Soc Nephrol*. 2007;18(4):1239-1245. doi:10.1681/ASN.2006111299.
21. Yadav P, Sathick IJ, Leung N, et al. Serum free light chain level at diagnosis in myeloma cast nephropathy—a multicentre study. *Blood Cancer J*. 2020;10(3):28. doi:10.1038/s41408-020-0295-4.
22. Sanders PW. Mechanisms of light chain injury along the tubular nephron. *J Am Soc Nephrol*. 2012;23(11):1777-1781. doi:10.1681/ASN.2012040388.
23. Katzmann JA, Kyle RA, Benson J, et al. Screening panels for detection of monoclonal gammopathies. *Clin Chem*. 2009;55(8):1517-1522. doi:10.1373/clinchem.2009.126664.
24. Herrera GA, ed. The Kidney in Plasma Cell Dyscrasias. Contributions to Nephrology. Vol 153. Basel, Switzerland: S. Karger AG; 2007.
25. Park S, Han B, Kim K, et al. Renal insufficiency in newly-diagnosed multiple myeloma: analysis according to International Myeloma Working Group consensus statement. *Anticancer Res*. 2014;34(8):4299-4306.
26. Qin X, Xu Y, An G, et al. The impact of renal function on prognostic value of $\beta 2$ -microglobulin of ISS stage system in multiple myeloma patients—clinical data analysis of 666 patients in a single center [in Chinese]. *Zhonghua Xue Ye Xue Za Zhi*. 2015;36(5):393-397. doi:10.3760/cma.j.issn.0253-2727.2015.05.008.
27. Korkmaz M, Aras B, Güneyli S, Yilmaz M. Clinical significance of renal cortical thickness in patients with chronic kidney disease. *Ultrasonography*. 2018;37(1):50-54. doi:10.14366/usg.17012.
28. Moghazi S, Jones E, Schroeppele J, et al. Correlation of renal histopathology with sonographic findings. *Kidney Int*. 2005;67(4):1515-1520. doi:10.1111/j.1523-1755.2005.00230.x.
29. Ahmed S, Bughio S, Hassan M, et al. Role of ultrasound in the diagnosis of chronic kidney disease and its correlation with serum creatinine level. *Cureus*. 2019;11(3):e4241. doi:10.7759/cureus.4241.
30. Quaia E, Bertolotto M. Renal parenchymal diseases: is characterization feasible with ultrasound? *Eur Radiol*. 2002;12(8):2006-2020. doi:10.1007/s00330-002-1360-z.
31. Bridoux F, Carron PL, Pegourie B, et al. Effect of high-cutoff hemodialysis vs conventional hemodialysis on hemodialysis independence among patients with myeloma cast nephropathy: a randomized clinical trial. *JAMA*. 2017;318(21):2099-2110. doi:10.1001/jama.2017.17924.
32. Leung N, Gertz MA, Zeldenrust SR, et al. Improvement of cast nephropathy with plasma exchange depends on the diagnosis and on reduction of serum free light chains. *Kidney Int*. 2008;73(11):1282-1288. doi:10.1038/ki.2008.108.