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Acute renal failure as a manifestation of multiple myeloma frequency and clinical implications

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Abstract--Objective: Aim was to determine the association and clinical implications of renal failure among patients of multiple

myeloma. Study Design: Prospective/observational study. Place and Duration: Diagnostic and research Laboratory Liaquat university of Medical and health sciences jamshoro Hyderabad. June 2021 to may 2022. Methods: Total 192 patients of multiple myeloma were presented in this study. Patients were enrolled after obtaining written consent detailing age, sex, and the presence or absence of any and all comorbidities. A serum creatinine level of 177 mol/L or above (>2 mg/dL) was considered indicative of renal failure. All the patients received chemotherapy for recovery. Response rate to chemo and survival among all patients were determined. SPSS 23.0 was used to analyze all data. Results: There were 106 (55.2%) males and 86 (44.8%) cases were females. Patients mean age was 51.6 ±13.46 years. Chronic renal disease, diabetes, hypercalcemia, dehydration, and the use of nephrotoxic medicines were all risk factors. We found renal failure in 43 (22.4%) cases. Patients without renal failure had higher response rate 90 (60.4%) to chemotherapy as compared to patients of renal failure 16 (37.2%). 13 (30.2%) cases were recovered from renal failure and mean time of survival was 3.3±3.18 years. Mortality was found in 22 (51.2%) among cases of renal function. Conclusion: Almost 22.4% of MM patients had renal failure. Renal failure patients who recovered lived longer. Renal function didn't alter response rate. Renal function recovery was affected by renal failure, hypercalcemia, and proteinuria. Survival was only affected by treatment response and renal failure severity.

Keywords--renal failure, multiple myeloma, mortality, risk factors, recovery.

Introduction

A hallmark of multiple myeloma is the uncontrolled growth of a single clone of plasma cells. It causes osteolytic bone lesions locally and systemic homogenous immunoglobulin or light chain synthesis to exert its effects systemically. Many patients with myeloma experience kidney complications, such as acute or chronic renal failure, nephrotic syndrome, non-nephrotic proteinuria, or tubular function deficits [1,2]. An indication of myeloma's presence, azotemia is both a major management challenge and a poor prognostic factor [3]. Besides infections, renal failure is the leading cause of death worldwide [4]. There has been no change in the prevalence of renal failure among myeloma patients over the past two decades, despite the fact that their overall survival has improved due to advancements in supportive treatment and the availability of powerful antibiotics and chemotherapeutic drugs [5]. In multiple myeloma, the particular mechanisms by which renal impairment develops are only partially understood.[4-6]

An approximate global five-year prevalence of 230,000 patients is estimated. There are reportedly five new instances for every hundred thousand people in the Western world when adjusted for age. Patients typically are diagnosed between the ages of 66 and 70, with 37 percent being under 65. Men seem to be slightly more likely to be diagnosed with MM than women, and MM is extremely

uncommon in those younger than 30. Despite the fact that familial cases of MM are extremely uncommon, they do occur. Compared to healthy controls, the risk of acquiring MGUS, MM, Waldenström macroglobulinemia, and chronic lymphocytic leukemia was found to be 2.8 times, 2.9 times, 4.0 times, and 2.8 times greater, respectively, in the families of patients with MGUS [7]. The CRAB characteristics, which include hypercalcemia, renal failure, anemia, and bone lesions, are utilized to diagnose MM when other symptoms are absent. Hypercalcemia and bone pain are hallmarks of this syndrome, which is caused by lytic bone lesions and elevated osteoclastic activity. About 73% of people with MM also have anemia when they appear. This case report focuses on renal failure, which is typically brought on by the accumulation of pathological light chains in the kidneys. About half of MM patients present with elevated creatinine. Renal impairment is a common initial manifestation of MM, however it is uncommon to be the only initial manifestation [8]. Taking a deeper look at the glomeruli and tubules via kidney biopsy is often necessary for diagnosing renal failure. It is possible to observe the tubules filled of proteins that clog the inside of the tubule when a patient has cast MM. Cast nephropathy is characterized by normal-appearing glomeruli in the kidney [9].

Conditions that complicate the treatment of patients with multiple myeloma include older age at presentation and multiple coexisting morbidities, such as hypertension, diabetes, or other chronic health conditions. Rajkumar and Dispenzieri (2008) Renal failure or the development of end-stage renal disease (ESRD) requiring dialysis can occur in patients with light chain cast nephropathy. In addition to multiple myeloma, other causes of kidney failure in patients with a suspected diagnosis of the disease include light chain amyloidosis (AL), light chain deposition disease (LCDD), either monoclonal immunoglobulin deposition disease (MIDD), and acute tubular necrosis (ATN) caused by nephrotoxic agents in the context of monoclonal gammopathy. According to research (Leung et al., 2008) Despite the variability of renal illness in patients with multiple myeloma, careful consideration must be given to therapy selection in order to slow the onset of end-stage renal disease (ESRD) and the need for dialysis, both of which are associated with decreased overall survival. To wit: (Blade et al., 1998; Blade & Rosinol, 2005).[10-12]

Patients at risk for kidney damage due to multiple myeloma can be identified by clinicians, who can then implement preventative and therapeutic measures; nonetheless, long-term unfavorable effects may still occur. Our mission is to provide guidance for the prevention and treatment of renal problems in individuals with multiple myeloma by detailing the effects of the disease and the importance of screening for it. These patients desperately need thorough screening for the onset of acute or gradual renal impairment so that they can receive treatment as soon as possible and avoid further consequences.

Materials and Methods

This prospective/observational study was conducted at Diagnostic and research Laboratory Liaquat university of Medical and health sciences jamshoro Hyderabad and comprised of 192 patients. Patients were enrolled after obtaining written consent detailing age, sex, and the presence or absence of any and all

comorbidities. Smouldering myeloma patients were excluded. All of the study participants were experiencing disease-related symptoms. The patients were categorised based on the Durie and Salmon stage system. To be diagnosed with renal failure, the serum creatinine concentration needed to be 177 mol/L or greater (2 mg/dL). Renal insufficiency could be reversed if serum creatinine levels were consistently lowered to below 133 mol/L (1.5 mg/dL).

Patients were given fluids and blood transfusions as necessary as part of a comprehensive plan of care. Treatment for hypercalcemia included a combination of saline solution, furosemide, and glucocorticoids to induce diuresis. In this stage of the disease, we did not give any of our patients bisphosphonates or calcitonin. Different chemotherapy cycles included vincristine sulphate, cyclophosphamide, melphalan, and prednisone (VCMP); alternating cycles of VCMP and vincristine, carmustine, doxorubicin hydrochloride (Adriamycin); and vincristine sulphate, Adriamycin, and dexamethasone phosphate (VAD; 1 patient). Due to their grave clinical condition, 5 patients were not treated at all, whereas 8 got either continuous low-dose alkylating drugs or prednisone alone. If no severe myelosuppression was seen in patients who recovered renal function after the first two cycles of chemotherapy, the doses of alkylating agents (such as melphalan and cyclophosphamide) and carmustine and Adriamycin were increased in subsequent courses. Dialysis was used as an active treatment option, alongside chemotherapy and supportive care. Dialysis was used to treat 24 individuals as a form of renal replacement treatment. Patients in this research who needed maintenance dialysis had previously been described, along with their results. In addition, plasmapheresis was used to treat 8 individuals. Multiple comparisons' statistical significance was evaluated using the X² and Fisher exact tests. Kaplan-Meier survival analyses were performed, and log-rank tests were used to compare survival rates between groups.

Results

There were 106 (55.2%) males and 86 (44.8%) cases were females. Patients mean age was 51.6 ±13.46 years. Chronic renal disease, diabetes, hypercalcemia, dehydration, and the use of nephrotoxic medicines were all risk factors. 88 patients had skeletal abnormalities, osteoporosis was found in 60 cases and 42 cases had lytic lesion.(table 1)

Table 1
Patients characteristics at start

Variables	Frequency (192)	Percentage
Mean age (years)	51.6 ±13.46	
Gender		
Male	106	55.2
Female	86	44.8
Risk Factors		
chronic renal disease	80	41.7
diabetes	37	19.3
hypercalcemia	30	15.6
dehydration	25	13.02

nephrotoxic medicines	20	10.4
Skeletal abnormalities		
Yes	88	45.8
No	104	54.2
Osteoporosis		
Yes	60	31.3
No	132	68.7
Lytic lesion		
Yes	42	21.9
No	150	78.1

We found renal failure in 43 (22.4%) cases and 149 (77.6%) patients were non-renal failure.(figure 1)

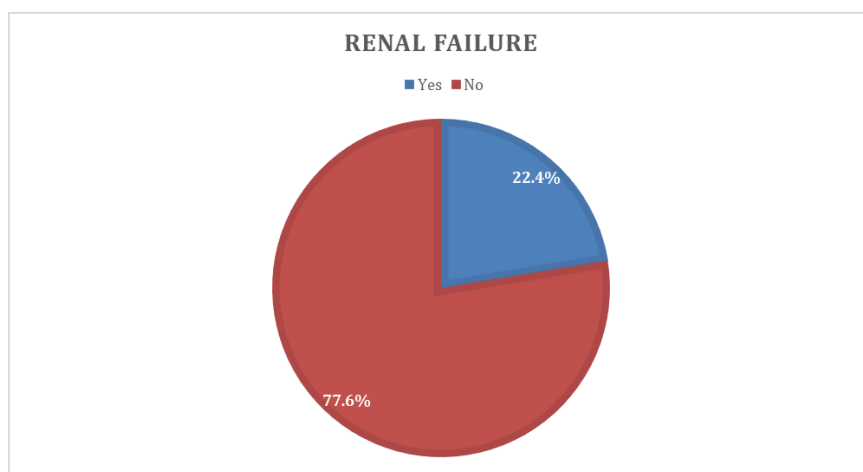


Figure 1. Frequency of renal failure

Patients without renal failure had higher response rate 90 (60.4%) to chemotherapy as compared to patients of renal failure 16 (37.2%).(table 2)

Table 2
Response rate to chemotherapy among all cases

Variables	Renal Failure (43)	Non-renal failure (149)
Chemotherapy Response rate		
Yes	16 (37.2%)	90 (60.4%)
No	27 (62.8%)	59 (39.6%)

Thirteen (30.2%) cases were recovered from renal failure and mean time of survival was 3.3 ± 3.18 years. Mortality was found in 22 (51.2%) among cases of renal function.(table 3)

Table 3
Outcomes among patients of renal failure

Variables	Frequency (43)	Percentage
Recovery		
Yes	13	30.2
No	30	69.8
Mean time of survival (years)	3.3±3.18	
Mortality		
Yes	22	51.2
No	21	48.8

Discussion

In roughly 20% of MM patients, renal insufficiency is present at diagnosis and is a major prognostic factor.[13] Myeloma kidney, produced by light-chain cast nephropathy, is the fundamental pathogenetic lesion leading to renal failure.[14] Variations in study populations and definitions of renal failure account for the large inter-series disparities in renal failure incidence and severity. At the time of diagnosis, 22.4% of the patients with MM in our tertiary hospital series had blood creatinine levels of 177 mol/L or higher (2 mg/dL). Renal insufficiency was found in 18% of a different big series from the same institution using the same definition for renal failure, while it was reported in 31% of a newly reported multicentric study⁴ using a creatinine limit of 133 mol/L (1.5 mg/dL) to define renal failure.[15]

The definition of renal involvement and the case-mix used in different studies contribute to this reported incidence variance. Employees who have reported larger numbers are more likely to have included those with less severe cases of azotemia.[16] Renal involvement preceded or corresponded with the diagnosis of myeloma in 41.7% of individuals who were admitted to our hospital after receiving a diagnosis of the disease. Several other workers have also reported experiencing this. Pozzi et al. found that in 78% of patients, renal failure was discovered at the same time as multiple myeloma.[17,18]

It is reasonable to obtain a rapid decrease in blood FLCs levels in individuals with multiple myeloma and other lymphoproliferative disorders when serum FLCs levels approach 500 mg/L [19]. This fast solution is based on the use of a very high dose of dexamethasone. However, patients with acute renal failure should avoid bisphosphonates because of the danger of further renal function impairment and the development of hypocalcemia with associated symptoms [20], despite their usefulness in controlling hypercalcemia caused by cancer treatment. We advocate reducing serum calcium levels in patients at risk for acute renal impairment prior to any contrast media testing, even though doing so is not mandated by the 2012 KDIGO AKI recommendation. Finally, high-risk multiple myeloma patients should avoid obtaining contrast media if they have been taking nonsteroidal anti-inflammatory drugs (NSAIDs), aminoglycosides, high-dose diuretics, antineoplastic medicines, or metformin within the previous 48 hours.

Few studies have examined treatment outcomes for people with MM and renal failure. Across trials, response rates ranged from 43% to 50%[21,22]. While 60.4%

of patients with normal renal function reacted in a previous study, only 37.2% of patients responded in our series. The median survival time for people with multiple myeloma with renal failure varies widely between studies.[23,24] Our patients had a median survival time of about 30 months, which is consistent with this estimate. Unfortunately, a low median survival has been consistently seen across all data in patients with MM and renal failure due to the high mortality rate of roughly 30% during the first 2 months of diagnosis. The requirement for dose adjustment of melphalan to avoid severe myelosuppression may suggest the danger of suboptimal treatment, hence it has been emphasized that melphalan and prednisone cycles are not the best option for patients with renal failure.

Conclusion

Almost 22.4% of MM patients had renal failure. Renal failure patients who recovered lived longer. Renal function didn't alter response rate. Renal function recovery was affected by renal failure, hypercalcemia, and proteinuria. Survival was only affected by treatment response and renal failure severity.

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