CORRELATION OF PROGNOSIS AND RENAL DYSFUNCTION WITH CLINICAL AND LAB PROFILE IN PLASMA CELL NEOPLASMS

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ABSTRACT

BACKGROUND

Plasma cell neoplasms are characterised by clonal proliferation and accumulation of immunoglobulin producing B cells that typically secrete a monoclonal immunoglobulin called M-protein.[1] Multiple myeloma is the commonest of the plasma cell neoplasms with an annual incidence of 1% of all malignancies and 10% of all haematological malignancies.[2] Indian incidence is approximately 6,000 new cases/year.[3] Renal complications develop in 20%-25% of myeloma.[4] Various new methods like cytogenetics and serum β_2 microglobulin estimation are ideal in measuring the prognosis of myeloma.[5] But, these are not available in most institutes. So, this study is done to assess the association of prognosis and renal dysfunction in plasma cell neoplasms based on routine clinical, hematological and biochemical variables.

MATERIALS AND METHODS

Patients were followed up for a maximum period of 3 years to evaluate the prognosis. Renal dysfunction was measured using serum creatinine and blood urea estimation.
Statistical Analysis- The data was analysed with the help of computer software SPSS version 18.

RESULTS

Fifty seven patients were newly diagnosed with plasma cell neoplasms. Male gender, thrombocytopenia, presence of recurrent infections and hyperphosphatemia were associated with bad prognosis. 28% of the study population had renal involvement at presentation. The factors which showed statistically significant association with renal dysfunction were serum calcium and serum phosphate.

CONCLUSION

Reasonably good assessment of prognosis and risk of renal failure can be made by evaluating routine parameters like gender, platelet count, serum phosphate, serum calcium and the presence of recurrent infections.

KEYWORDS

Plasma Cell Neoplasms, Multiple Myeloma, Prognosis, Renal Insufficiency.

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BACKGROUND

Plasma cell neoplasms are a spectrum of diseases characterised by clonal proliferation and accumulation of immunoglobulin producing terminally differentiated B cells that typically secrete a single homogenous (monoclonal) immunoglobulin called a paraprotein or M-protein. They include multiple myeloma, Monoclonal Gammopathy of Undetermined Significance (MGUS), Primary amyloidosis, plasma cell leukaemia, heavy chain and light chain disease.[1] The outcome of myeloma patients are highly heterogeneous with median survival of approximately 6-7 years.[6] This is the main reason for extensive investigation on prognostic factors and many parameters related to prognosis have been described. Serum β_2 microglobulin, cytogenetics, etc. are ideal in measuring the prognosis of myeloma, but these are not available in most institutes. Renal dysfunction commonly develops in myeloma either at the time of presentation or sometime during the clinical course and is a common cause of death. So, this study is done to assess the association of prognosis and renal dysfunction in plasma cell neoplasms based on routine clinical and biochemical variables.

Aims and Objectives

1. To assess the influence of clinical, biochemical and haematological parameters in the prognosis of plasma cell neoplasms.

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2. To determine the association between laboratory parameters and renal involvement in plasma cell neoplasms.

Setting and Design- This was a prospective study involving all consecutive newly-diagnosed cases of plasma cell neoplasms that came to Government Medical College Hospital, Kozhikode, during the period of 3 years, from March 2009 to February 2012.

MATERIALS AND METHODS

All consecutive newly-diagnosed cases of plasma cell neoplasms registered in Government Medical College, Kozhikode, during the period March 1, 2009, to February 29, 2012, were taken for this study. All patients were diagnosed as per WHO diagnostic criteria[1] for plasma cell neoplasms. The biochemical parameters noted were serum creatinine, blood urea, total protein, albumin/globulin ratio, serum calcium, serum albumin and serum phosphate. Platelet counts of these patients were categorised into four groups, less than 50,000, 50,000-1,50,000-4,00,000 and above 4,00,000/mm^3. Other laboratory parameters were also categorised to normal, high/low based on the standard normal values. Patients were followed up for a maximum period of 3 years to evaluate the prognosis. The number of patients alive at 6 months, 1 year and 3 years were noted. Age, sex, presence or absence of recurrent infections, various haematological and biochemical parameters of these patients were correlated with prognosis and risk of renal failure.

Inclusion Criteria

All patients registered at Government Medical College, Kozhikode, during the period of March 1, 2009, to February 29, 2012, with diagnosis of plasma cell neoplasms.

Exclusion Criteria

Patients already on treatment and who discontinued treatment were excluded.

Statistical Analysis

Data was analysed with the help of computer software SPSS version 18. Qualitative variables were presented as frequencies and percentages. Association of prognostic factors was tested using Chi-square test. A 'p' value of ≤0.05 was considered as statistically significant.

Ethics- This study has been approved by Institutional Ethics Committee of Government Medical College, Kozhikode.

RESULTS

A total of 57 patients were diagnosed to have plasma cell neoplasms in Medical College, Kozhikode, during the study period. This included predominantly (53 cases) multiple myeloma and 3 cases of MGUS and one case of plasma cell leukaemia. The mortality at the end of study period was 33% as shown in Figure 1.

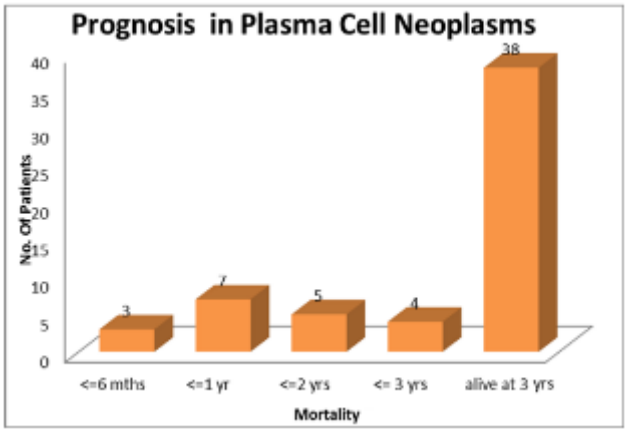

Figure 1. Bar Chart Showing Prognosis in Plasma Cell Neoplasms

Association of Prognosis with Clinical and Lab Parameters

The association between age and prognosis was not statistically significant (Table 1).

Age	Prognosis at End of Study Period		Total
	Alive	Died	
20-29 years	1 (100%)	0	1
30-39 years	1 (100%)	0	1
40-49 years	6 (86%)	1 (14%)	7
50-59 years	10 (59%)	7 (41%)	17
60-69 years	11 (85%)	2 (15%)	13
70-79 years	6 (50%)	6 (50%)	12
80-89 years	3 (50%)	3 (50%)	6

Table 1. Prognosis in Plasma Cell Neoplasms Among Different Age Groups

Chi-square value 6.748; pvalue-0.345.

Of the 29 male patients, 15 were alive at the end of study period (52%), while 23 of the 28 female patients included (82%) were alive. The association between gender and prognosis was statistically significant (Table 2).

Sex	Prognosis at End of Study Period		Total
	Alive	Died	
Male	15 (52%)	14 (48%)	29
Female	23 (82%)	5 (18%)	28

Table 2. Sex and Prognosis

Chi-square value 5.932; p value=0.015.

81% of those patients without infections survived while only 40% of those patients with recurrent infections survived at the end of the study period. The correlation between presence of infection and prognosis was statistically significant as the 'p' value was <0.05 (Table 3).

Recurrent Infections	Prognosis at End of Study Period		Total
	Alive	Died	
No	38 (81%)	9 (19%)	47
Yes	4 (40%)	6 (60%)	10

Table 3. Recurrent Infection Versus Prognosis

Chi-square value 7.096; p value=0.008.

55 patients (96%) presented with anaemia, but there was no statistically significant correlation between haemoglobin levels and prognosis (Table 4).

Hb	Prognosis at End of Study Period		Total
	Alive	Died	
Normal	1 (50%)	1 (50%)	2
Low	41 (75%)	14 (25%)	55
Table 4. Haemoglobin Versus Prognosis			

Chi-square value 1.036; p value=0.309.

As the 'p' value is <0.05, the association between platelet count and prognosis was statistically significant (Table 5).

Platelet Count	Prognosis at End of Study Period		Total
	Alive	Died	
50,000/mm^3	2 (22%)	7 (78%)	9
50,000-1.5 lakhs/mm^3	7 (58%)	5 (42%)	12
1.5-4 lakhs/mm^3	29 (83%)	6 (17%)	35
More than 4 lakhs/mm^3	0 (0%)	1 (100%)	1
Table 5. Platelet Count Versus Prognosis			

Chi-square value 14.504; p value=0.002.

As the 'p' value is <0.05, the association between serum phosphate levels and prognosis was statistically significant (Table 6).

S. Phosphate	Prognosis at the End of Study Period		Total
	Alive	Died	
High (>4.5 mg%)	1 (25%)	3 (75%)	4
Normal (2.5-4.5 mg%)	41 (77%)	12 (23%)	53
Table 6. S. Phosphate Versus Prognosis			

Chi-square value 5.258; p value=0.022.

There was no statistically significant correlation between serum levels of calcium and albumin with the disease prognosis (Tables 7, 8).

S. Calcium	Prognosis at End of Study Period		Total
	Alive	Died	
High (>11 mg%)	3 (100%)	0	3
Normal (9-11 mg%)	24 (65%)	13 (35%)	37
Low (<9 mg%)	11 (65%)	6 (35%)	17
Table 7. S. Calcium Versus Prognosis			

Chi-square value 1.583; p value=0.453.

S. Albumin	Prognosis at End of Study Period		Total
	Alive	Died	
Low (<3.5 g%)	35 (66%)	18 (34%)	53
Normal (3.5-5.5 g%)	3 (75%)	1 (25%)	4
Table 8. S. Albumin Versus Prognosis			

Chi-square value 0.134; p value=0.714.

28% (16 patients) of the study population had renal involvement at presentation based on serum creatinine levels. 50% of patients with high serum creatinine expired during the study period, while only 27% of patients with normal serum creatinine expired. But, there was no statistically significant correlation between serum creatinine and prognosis (Table 9).

S. Creatinine	Prognosis at End of Study Period		Total
	Alive	Died	
High (>1.4 mg%)	8 (50%)	8 (50%)	16
Normal (0.6-1.3 mg%)	30 (73%)	11 (27%)	41
Table 9. S. Creatinine Versus Prognosis			

Chi-square value 2.780; p value=0.095.

One of the patients presented with unexplained renal failure and underwent renal biopsy to arrive at a diagnosis. Histopathology showed cast nephropathy with fractured casts showing mononuclear and giant cell reaction as shown in Figure 2. On further clinical and laboratory work up, the case was diagnosed as multiple myeloma.

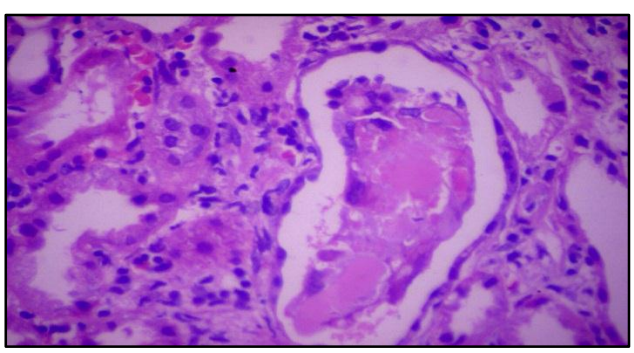

Figure 2. Renal Tubules with Fractured Casts and Mononuclear Cell Reaction in Myeloma

Association of Renal Failure with Clinical and Lab Parameters

The association between serum creatinine and serum phosphate and between serum creatinine and calcium were statistically significant. But, the relation between serum creatinine and albumin was not statistically significant (Table 10).

S. Creatinine	S. Calcium			S. Albumin			S. Phosphate		
	Normal	Low	High	Normal	Low	High	Normal	Low	High
Normal (41)	31 (75.5%)	8 (19.5%)	2 (5%)	4 (10%)	37 (90%)	0	41 (100%)	0	0
High (16)	6 (37.5%)	9 (56.5%)	1 (6%)	1 (6%)	15 (94%)	0	12 (75%)	0	4 (25%)
Table 10. Correlation of Serum Creatinine with Serum Calcium, Albumin and Phosphate									

S. creatinine and S. calcium; Chi-square 7.824; p value=0.02.
S. creatinine and S. albumin; Chi-square is 0.18, p value=0.674.
S. creatinine and S. phosphate; Chi-square 11.024, p value=0. 001.

DISCUSSION

The mean survival period of patients with plasma cell neoplasms in the present study was 30.4 months, which closely relates to the mean survival period in the study conducted by Robert A Kyle et al.[7] In our study, the risk factors, which had statistically significant association with prognosis in plasma cell neoplasms were gender, presence of infections, platelet counts and the serum phosphate levels. Males showed poorer survival than females, which was similar to other studies.[8] But, in the study by Boyd et al, female gender was associated with inferior overall survival (median 44.8 months female vs. 49.9 months male, p=0.020).[9] Hyperphosphatemia and thrombocytopenia also showed a bad prognosis. This was comparable with earlier studies.[10,11] Patients with recurrent infections had a decreased survival. 81% of those patients without recurrent infections survived, while only 40% of those patients with recurrent infections survived at the end of the study period. The study by Blimark et al also showed that infections are a major cause of morbidity and mortality in patients with multiple myeloma.[12]

Earlier studies have shown that risk factors like increased age, associated renal failure and low serum albumin levels correlate with prognosis.[11,13] In this study, there were very few patients in the younger age groups since myeloma is more common in middle age and elderly. So, the association between age and prognosis was not statistically significant. Haemoglobin, serum albumin and serum calcium levels also did not show a correlation with prognosis.

28% of plasma cell neoplasms in our study had renal failure at presentation. The Nordic Myeloma Study Group evaluated renal function by serum creatinine concentration in 1353 cases of multiple myeloma and found that 31% had renal failure at the time of diagnosis.[14] In our study, 50% of patients with high serum creatinine expired during the study period while only 27% of patients with normal serum creatinine expired. But, there was no statistically significant correlation between serum creatinine and prognosis probably due to the small sample size. The three most common forms of monoclonal immunoglobulin mediated kidney disease are cast nephropathy, Monoclonal Immunoglobulin Deposition Disease (MIDD) and amyloidosis.[15] Cast nephropathy is characterised by the presence of fractured casts formed of Free Light Chains (FLC) and uromodulin.[16] These casts precipitate out in the distal tubules resulting in tubular obstruction and associated tubulointerstitial inflammation. Serum calcium and phosphate were found to be statistically associated with serum creatinine values. But, the hypocalcaemia found in the majority of our cases with high serum creatinine maybe due to the associated hypoalbuminaemia.[17]

Summary

This is a hospital-based observational study. It included 57 patients who presented to Government Medical College, Kozhikode, and were diagnosed to have plasma cell neoplasms. Mortality at the end of the study period was 34%. In the study population, 28% of patients had renal involvement at presentation of which 50% expired during the study period. Male sex, presence of recurrent infections, hyperphosphatemia and thrombocytopenia carried a bad prognosis. Serum phosphate and serum calcium were found to be significantly associated with serum creatinine values.

CONCLUSION

Though the exact prognostication and risk of renal dysfunction in plasma cell neoplasms require expensive new modalities, a rough reasonably good assessment of prognosis and risk of renal failure can be made by evaluating routine parameters like gender, platelet count, serum phosphate and serum calcium and the presence of recurrent infections.

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