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RESEARCH ARTICLE

Outcomes of Patients with Multiple Myeloma in Middle Euphrates Region of Iraq: Data from Developing Country

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Abstract

Background: Multiple myeloma (MM) is a B cells neoplasm characterized by plasma cells clonal proliferation. **Aims:** The aim of this study was to evaluate incidence, prevalence and pattern of multiple myeloma (MM) in Middle Euphrates region of Iraq. **Materials and Methods:** A retrospective descriptive conducted at Al-Hussein center in Karbala province of Iraq between February 2012 and February 2020. **Results:** A total of 78 patients with MM were included in this study, median age at presentation was 59.8 years, M:F ratio was 0.85:1. The most frequent presenting complain was bony lesions in 87.18% of patients, IgG was the most frequent paraprotient in 61.53% and VRD was the most common used protocol in 37.18% . Survival rate was higher in younger & female patients, while there was no correlation between myeloma defining events and early death in our study. **Conclusion:** MM presenting age in our region was close to other parts of Iraq and neighboring countries but younger than western countries with female predominance. Giving that the majority of the patients presented with advance stage disease, therefore raising awareness of early symptoms is recommended for early diagnosis and proper management.

Keywords: Multiple myeloma- Middle Euphrates Region- Iraq

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Introduction

Multiple myeloma (MM) is a malignant hematological disease characterized by the irregular proliferation of clonal plasma cells in the bone marrow [1]. These clonal plasma cells secrete large quantities of monoclonal immunoglobulin into the serum and/or urine, leading to significant morbidity due to end-organ destruction [2].

The etiology of MM is unclear but it commonly occur among farmers, wood workers, leather workers, petroleum products exposed workers and occupations associated with radiation. Several studies suggested that various etiological factors may have played a role in MM etiology such as viral infections, inflammatory disorders, autoimmune diseases, allergic diseases & family history [3-4].

Early recognition of clinical symptoms is an important factor for early management and preventing irreversible complications. Several criteria have been used to diagnose MM & distinguish it from other plasma cell diseases [5].

The following criteria must be fulfilled:

A. Clonal bone marrow plasma cells ≥ 10% or biopsy-proven bony or extramedullary plasmacytoma

B. Any one or more of the following myeloma- defining events:

1. Hypercalcemia: Serum calcium > 0.25 mmol/L (>1 mg/dL) higher than the upper limit of normal or >2.75 mmol/L (> 11 mg/dL).

2. Renal insufficiency: Creatinine clearance < 40 mL/ min or serum creatinine > 177 mmol/L (> 2 mg/dL).

3. Anemia: Hemoglobin value <10 g/dL or hemoglobin > 2 g/dL below the lowest limits of normal hemoglobin levels.

4. Bone lesions: One or more osteolytic lesions on skeletal radiography, CT or PET/CT.

5. Clonal bone marrow plasma cell ≥ 60%.

6. Involved: uninvolved serum free light chain (FLC) ratio ≥ 100 and the involved FLC level must be 10 mg/

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dL or higher.

7. More than one focal lesion on MRI studies (≥5 mm in size) [6].

Until 2000, the mainstays of MM therapy were alkylating agents, corticosteroids and high-dose chemotherapy with autologous stem cell transplantation (ASCT). Recently, thalidomide, bortezomib, lenalidomide, carfilzomib and pomalidomide are emerged as effective agents that dramatically improved clinical outcomes [7].

This was the first statistical study of MM in Middle Euphrates region of Iraq, it can help provide basic information, assess progress in recent years and develop future myeloma treatment strategies in this area of our county.

Materials and Methods

This was a retrospective, descriptive study conducted in Al-Hussein cancer center in Karbala province of Iraq on MM patients diagnosed between February 2012 to February 2020. This center was established in November 2011 with oncology & hematology wards. It covers not only Karbala population but other patients from Middle Euphrates region of Iraq who are referred to this center for solid & hematological malignancies treatment [8-9]. All patients had full blood & biochemistry profile especially complete blood count, renal functions tests, serum and urine electrophoresis, serum calcium, skeletal survey and bone marrow aspirate with biopsy. Data also provide information about sex, age, occupational history and treatment plan. Patients with inconclusive results were excluded from the study. The study protocol was approved by Ethical Committee of Teaching Hospital in Karbala , Iraq.

The statistical package for social sciences (SPSS) for windows, version 24 was used for entering, managing and analysis of data. Findings were presented in Tables and figures using MS-office software version 2013. P-values of 0.05 or less were regarded as statistically significant.

Results

Seventy eight patients were enrolled in the study. Median age at presentation was 59.8 years (range 33-91 years). Thirty six patients (46.15%) were males and 42 (53.85%) were females with M:F ratio 0.85:1.

Regarding myeloma-defining events, bony lesions presented in 68 patients (87.18%) followed by anemia in 58 patients (74.36%), renal impairment in 19 patients (24.36%) and hypercalcemia in 14 patients (17.95%).

The most common treatment protocol in our center was VRD protocol in 29 patients (37.18%) followed by VD protocol in 21 patients (26.92%), VCD protocol in 12 patients (15.38%), VTP protocol in 9 patients (11.54%), melphalan & prednisolone in 4 patients (5.13%), supportive treatment in 2 patients (2.57%) and VAD protocol in one patient (1.28%) as shown in (Table 1).

The paraprotein types of MM patients showed that the most common type was IgG in 48 patients (61.53%) followed by IgA in 15 patients (19.24%). Regarding

Table 1. Baseline Characteristics of MM Patients in Middle Euphrates Region of Iraq (N=78)

Characteristics	N (%)
Age in years	
Median	59.8
Range	33-91
Gender	
Male	36 (46.15)
Female	42 (53.85)
Myeloma-defining events	
Anemia	58 (74.36)
Bony lesions	68 (87.18)
Hypercalcemia	14 (17.95)
Renal impairment	19 (24.36)
Treatment protocols	
VRD	29 (37.18)
VD	21 (26.92)
VCD	12 (15.38)
VTP	9 (11.54)
Melphalan & prednisolone	4 (5.13)
VAD	1 (1.28)
Supportive	2 (2.57)

VRD, bortezomib; lenalidomide; dexamethasone; VD, bortezomib; dexamethasone; VTP, bortezomib; thalidomide; prednisone; VCD, bortezomib, cyclophosphamide, dexamethasone; VAD, vincristine; doxorubicin; dexamethasone.

Immunofixation, 45 patients (57.70%) had kappa chain, 29 (37.17%) had lambda chain and 4 (5.13%) were non secretary as shown in Figure 1.

The mean duration of follow-up was 24.67 months. A total of 16 patients (20.51%) died during the study period as shown in Figures 2 and 3. Survival rate was higher in patients < 50 years 83.33% versus 66.67% in patients > 70 years and among females (83.33% versus 75.00% in males) , and these differences were statistically significant (P value = 0.013 and 0.031, respectively). On the other hand, there was no correlation between myeloma defining events and treatment protocols on survival (P value > 0.05 each) (Table 2).

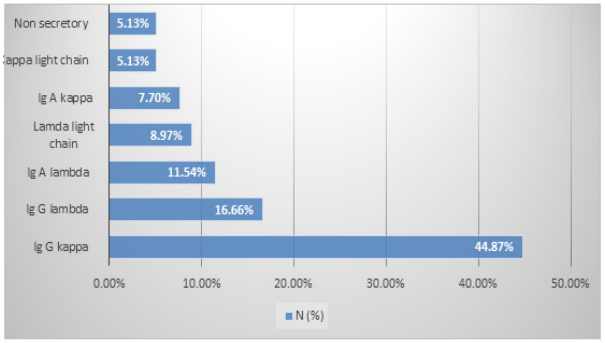

Figure 1. Types of Paraproteins

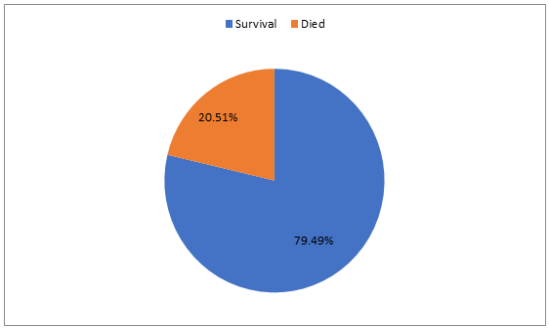

Figure 2. Survival and Death Rates

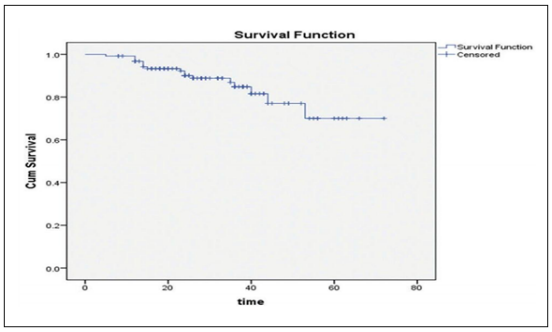

Figure 3. Mean Survival Time

Discussion

MM accounts for about 1% of all cancers and approximately 10% of all hematologic malignancies. More than 30,000 new cases are diagnosed in the US per year and more than 12,000 patients have died from the disease, while in Iraq MM accounts for around 1.08 % of cancer patients [10-11]. It is generally more common in men & among African-Americans and median age of patients was around 65 years [12].

In the present study, the median age at presentation was 59.8 years which was close to median age in other parts of Iraq, India, China and Turkey [12-15]. While mean age in US was a decade older than ours[16]. Interestingly, in

Table 2. Survival Rate Based on the Clinical Characteristics and Treatment Protocols

Characteristic	N (62) Survive	N (16) Died	P value
Age in years			
<50	10 (83.33%)	2 (16.67%)	0.013*
50-59	22 (81.48%)	5 (18.52%)	
60-69	20 (83.33%)	4 (16.67%)	
≥70	10 (66.67%)	5 (33.33%)	
Gender			
Male	27 (75.00%)	9 (25.00%)	0.031*
Female	35 (83.33%)	7 (16.67%)	
Myeloma-defining events			
Anemia			0.249
Yes	44 (75.86%)	14 (24.14%)	
No	18 (90.00%)	2 (10.00%)	
Bony lesions			0.435
Yes	54 (79.41%)	14 (20.59%)	
No	8 (80.00%)	2 (20.00%)	
Hypercalcemia			0.381
Yes	11 (78.57%)	3 (21.43%)	
No	51 (79.69%)	13 (20.31%)	
Renal impairment			0.27
Yes	17 (89.47%)	2 (10.53%)	
No	45 (76.27%)	14 (23.73%)	
Treatment protocols			
VD	18 (85.71%)	3 (14.29%)	0.143
VTP	3 (33.33%)	6 (66.67%)	
VRD	29 (100.00%)	0 (0.00%)	
Melphalan & prednisolone	2 (50.00%)	2 (50.00%)	
VCD	9 (75.00%)	3 (25.00%)	
VAD	1 (100%)	0 (0.00%)	
Supportive	0 (0.00%)	2 (100%)	

* significant differences (P ≤ 0.05); VD, bortezomib, dexamethasone; VTP, bortezomib, thalidomide, prednisone ;VRD, bortezomib, lenalidomide and dexamethasone; VCD, bortezomib, cyclophosphamide, dexamethasone; VAD, vincristine, doxorubicin, dexamethasone.

our center MM was more common in females than males, that was inconsistent with previous studies conducted in north Iraq, Turkey,China and US [12,14,16,17].

Clinical presentations can be highly varied among patients, in our region bony lesions were the most common myeloma-defining event , same results in India, Iran and Turkey while in Africa & US anemia was the most common one [14,16,18-20].The most frequent monoclonal protein in our patients was IgG, which was consistent with previous studies in north Iraq, US, China and Turkey [12,14,16,17,21].

During the past decade, the survival rate of MM patients was significantly increased. But the median overall survival was less than five years [22]. In the present study, overall survival rate was high 79.49%, this may be explained by short follow-up period and a small sample size. Survival rate was greater in young patients, same results were obtained from a study conducted at 17 institutions from North America, Europe and Japan where younger myeloma patients were more favorable features and showed better survival [23]. On the other hand, in our study survival was better in female, same results were obtained from a study done by Derman et al., but disagreed with previously published data suggesting no difference in survival outcomes by sex [24-25].

There was no correlation between myeloma defining events and survival in our patients, which was inconsistent with previous studies conducted in China, Japan, Greece and Africa where survival rate was decreased in patients with myeloma defining events [12, 26-28].

Cancer patients tend to present with heterogonous presentations and complications making treatment of those patients as a major concern. Detection of the disease in its early stages before the appearance of signs & symptoms can significantly improve outcomes [29-35]. Treatment of MM is a great challenge to the health system with different treatment protocols. The advent of thalidomide, lenalidomide, and bortezomib changed the standard of treatment and improved the survival of MM patients [36]. In our center VRD protocol (bortezomib, lenalidomide and dexamethasone) was the commonly used regimen. This protocol became as standard of care in many centers with successful results [37]. In the present study, survival rate improved in patients used VRD protocol compared to other protocols , but this result was statistically not significant.

In conclusion, the results of this study showed that Iraqi patients with multiple myeloma were younger than patients in western countries. Most of patients presented with bony lesions in the late stages. IgG was the most frequent paraprotein in the patients. VRD protocol was the most commonly used protocol with good outcomes. Survival rate was higher in younger & female patients, while there was no correlation between myeloma defining events and early death in our study. Future studies in other parts of Iraq with a larger sample size & longer follow up period are recommended to understand MM pattern in our war- torn country.

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