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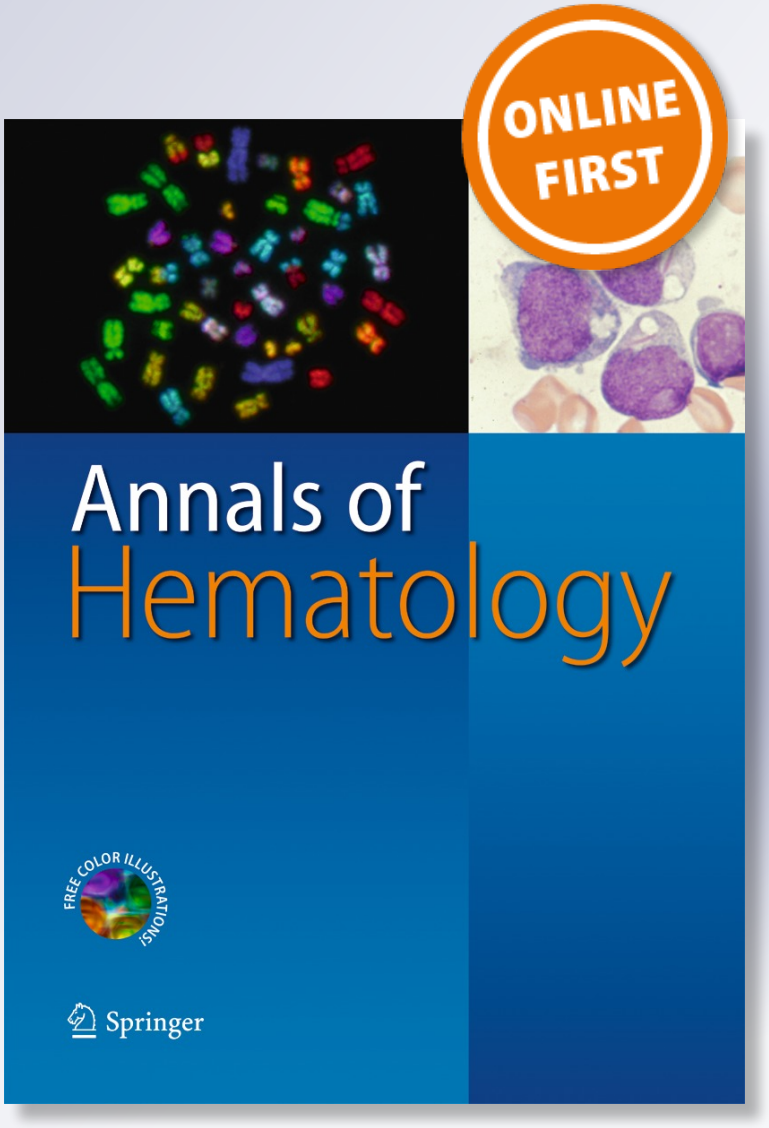

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ORIGINAL ARTICLE

Multiple myeloma: a descriptive study of 217 Egyptian patients

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Abstract Multiple myeloma is a neoplasm of plasma cells that results in the overproduction of light and heavy chain monoclonal immunoglobulins. The incidence rate increases with age, particularly after 40 years, and is higher in men. To determine the clinical and laboratory characteristics and survival of diagnosed Egyptian multiple myeloma patients admitted to the Haemato-Oncology Department between 2000 and 2010. Records of all patients in whom multiple myeloma was diagnosed at the Kasr Al Aini Hospital between 2000 and 2010 were included in this retrospective study. The mean age of patients was 58.5 years (range, 27–80 years). Fifty-nine percent were males. The majority of patients (73 %) had an immunoglobulin G monoclonal band and 70 % were Kappa chain-positive. Mean overall survival was 37.5 months (range, 1–84 months). Survival analysis was statistically insignificant with respect to age, sex, International Staging System and type of treatment ($p>0.05$). Our records were largely comparable to those reported in Chinese studies but different from those noted in Western and Arabic countries.

Keywords Myeloma · Chemotherapy · Epidemiology

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Introduction

Multiple myeloma (MM) is a neoplasm of plasma cells that results in the overproduction of light and heavy chain monoclonal immunoglobulins. Its incidence increases with age, particularly in people more than 40 years of age and is higher in men [1].

The cause of MM may be attributed to exposure to radiation, herbicides, insecticides, benzene, and other organic solvents. MM has also been reported in familial clusters of two or three first-degree relatives and in identical twins [2]. Older age, male gender, black race, family history of the disease, and monoclonal gammopathy of undetermined significance (MGUS) are all risk factors [3].

The most frequent cytogenetic abnormalities in MM include deletion of chromosomes 13 and 17, as well as immunoglobulin heavy chain rearrangement [4]. Monosomy or deletion of chromosome 13 was found to be associated with poor prognosis [5, 6]. Avet et al. [7] also reported that chromosome 13 deletions probably mark the transformation from MGUS to overt MM.

In this retrospective study, we review the epidemiological features and survival of multiple myeloma patients diagnosed and treated in the period between 2000 and 2010 in the Haemato-Oncology Unit of Kasr Al Aini, the largest tertiary hospital in Egypt, and compare our results with those from similar institutions in other countries.

Patients and methods

Ethical approval for this study was obtained from the Research Ethical Committee. The records of all patients in whom multiple myeloma initially diagnosed at Kasr Al Aini Hospital between 2000 and 2010 were reviewed. The diagnosis of MM was revised according to International Myeloma Working Group criteria [8]. Patients with plasma cell reactions to

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connective tissue disorders, liver disease, metastatic carcinoma, or chronic infections were excluded. Patients with MGUS, smoldering multiple myeloma, solitary plasmacytoma, and plasma cell leukemia were also excluded. The age, sex, and type of immunoglobulin heavy and light chains were determined using gel agar immunoelectrophoresis. Risk assessment was reviewed by determining albumin and B2 microglobulin. Initial treatments and survival data of patients were recorded. Fluorescent in situ hybridization (FISH) was used to carry out a cytogenetic analysis of 13q-.

Statistic analysis

SPSS version 17 was used to calculate the mean, median, and standard error (SE) of all parametric variables; and to conduct *T* tests for comparison of means; and z tests for nonparametric variables; ANOVAs to compare differences between group means; and Kaplan–Meier survival curves for overall survival analysis and Spearman's test for correlation analysis.

Results

Our study is a retrospective study that included 217 Egyptian patients with multiple myeloma diagnosed and treated between 2000 and 2010 at the Kasr Al Aini Hospital, Cairo.

Demographic and laboratory data are shown in Table 1. The mean age was 58.5 years (range, 27–80 years). Fifty-nine percent of the patients were male; 41 % were female. With respect to the immunoglobulin subtypes of myeloma, 29 patients (12.1 %) had light-chain myeloma and 38 (17.5 %) had IgA. Of the patients, 142 (73 %) had an immunoglobulin G (IgG) monoclonal band while 12 (5 %) had an IgM monoclonal band. Of the patients, 151 (70 %) were Kappa chain-positive and 66 (30 %) were lambda positive.

Survival analysis was conducted for 116 patients. Median overall survival was 37.5 months (range, 1–84 months). Thirty-one patients (27 %) were classified as International Staging System (ISS) stage 1 and had a median survival of 21.9 [SE=13.8]months. Seventy-eight patients (67 %) with ISS stage 2 had a mean survival of 20.5 (SD=15.9)months. Seven patients (6 %) were of ISS stage 3 and had a median survival of 16.6 months (SE=14.8).

An ANOVA of group differences with respect to age, sex, and ISS was carried out. No statistical difference was found. The survival analysis was not statistically significant ($p>$-0.05). Figure 1 demonstrates the survival difference between ISS stage (p=0.4). Figures 2 and 3 compare the survival difference between the two age groups (at or below 50 and above 50 years) and sex, respectively. Neither was statistically significant ($p>0.05$). Conventional cytogenetics results were available from 40 patients. Twelve patients (30 %) were established as being 13q- by the FISH technique.

Table 1 Demographic and laboratory data of patients with multiple myeloma

Factor	Number of patients	Percentage
Bodily pains	152	70
Splenomegaly	15	7
Lymphadenopathy	6	3
Hyperviscosity symptoms	22	10
Residence in rural areas	130	60
Smoking	98	45
Sex (male/female)	128, 89	59, 41
Age group (years)		
<40	8	4
40–49	20	9
50–59	85	39
60–69	82	38 %
70–79	20	9
≥80	2	1
Immunoglobulin electrophoresis:		
Light chain	26	12
Ig G myeloma	158	73
Ig M myeloma	11	5
Ig A myeloma	22	10
Kappa chain	151	70
Lambda chain	65	30
Hypercalcemia	86	40
Anemia (HB<10 g/dl)	206	95
Creatinine>1.5 mg/dl	65	30

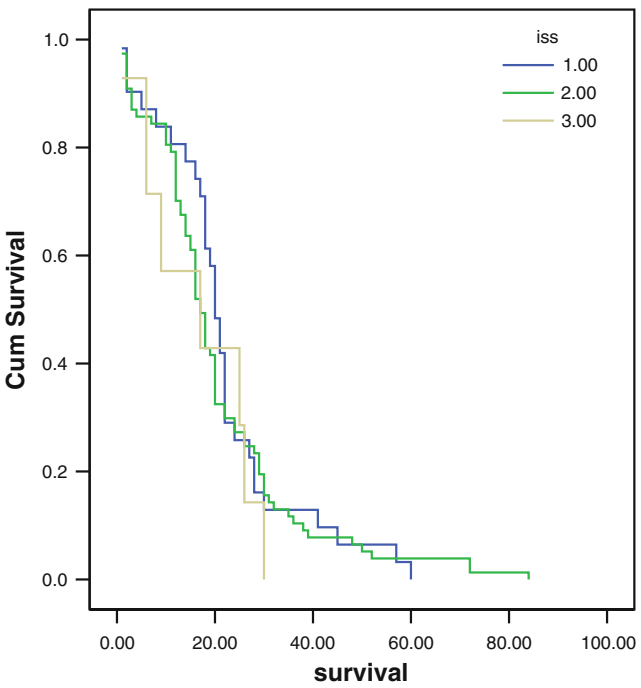

Fig. 1 Survival according by ISS score

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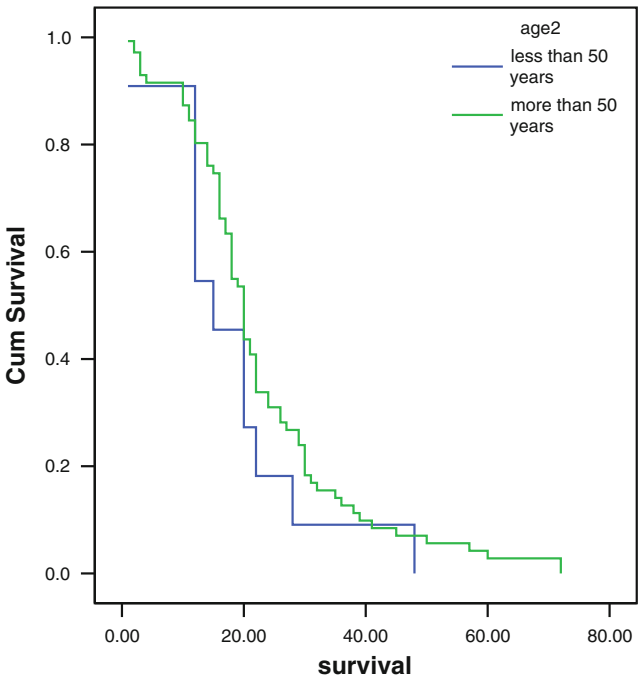

Fig. 2 Survival analysis by age group

The general treatment in our unit is with Endoxan/steroids or Melphalan/steroids. Median overall survival was 50.5 (SE=19.0)months. Other lines of treatments including Thalidomide (either alone or added to previous regimens), vincristine-doxorubicin (Adriamycin)-dexamethasone (VAD) regimen or velcade are given to a few patients when available within a clinical trial or by donation. Survival analysis by treatment subtype was statistically insignificant (Fig. 4). Table 2 demonstrates the median overall survival by treatment subtype other than Melphalan/steroids or Endoxan/steroids.

Discussion

Our study aimed to highlight the demographic and laboratory features of MM in Egyptian patients and to compare our results with those from other populations. The study included more than 200 MM patients who presented at the Kasr Al Aini hospital between 2000 and 2010.

The mean age of the studied group was 58.5 years (range, 27–80 years), which is similar to that reported in a Chinese study, but much younger than reported from western countries [9, 10].

For example, considering age-adjusted incidence rates by age group in the USA, multiple myeloma is rarely diagnosed before the age of 40 years, after which the incidence increases rapidly until 84 years of age, and then declines [1, 11]. The median age in England (Thames region) was 72 years [12] and a Swedish study reported a median age of 72 years [13]. The median ages in Tunisian, Saudi Arabian, Moroccan, and Bulgarian studies were 64 years [14], 56 years [15], 59 years [16], and 62 years [17], respectively.

There was a higher percentage of males than females (59 vs. 41 %) with MM. This was similar to what was reported in the South Thames area epidemiological study, and the Chinese and Moroccan studies [9, 12, 16]. Our results were

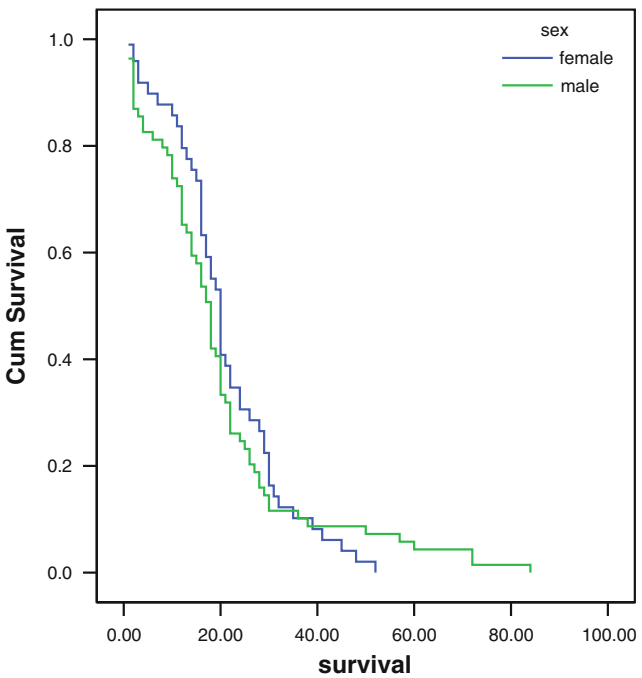

Fig. 3 Survival analysis by sex

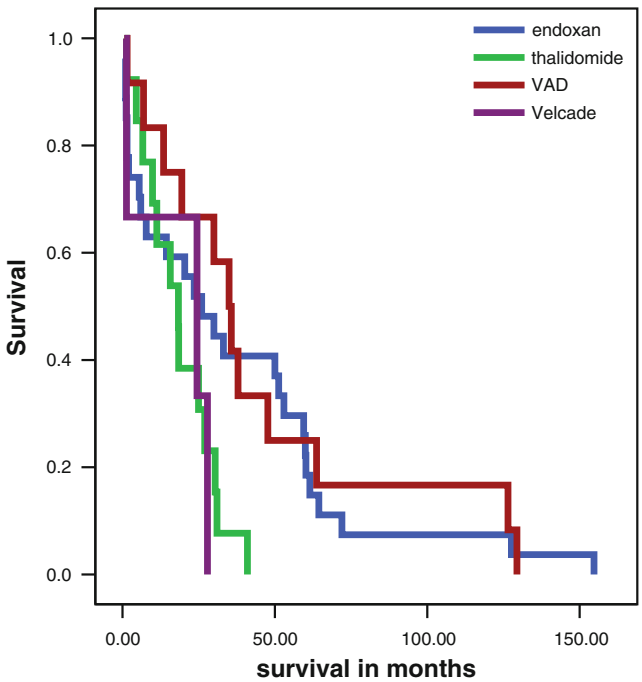

Fig. 4 Survival by treatment regimen

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Table 2 Frequencies of treatments other than Endoxan or Melphalan given to MM patients

Treatment	Number of patients (%)	Survival in months (mean±SE)
VAD	12 (22)	47.4±9.8
Velcade	3 (5)	30.9±8.4
Thalidomide	13 (24)	25.5±3.8

similar to those of the Mayo Clinic and Los Angeles studies, in which 59 % of 1,072 patients were male [18, 19]. US Surveillance Epidemiology and End Results Program (SEER) data from 1992 to 1998 indicated a male/female ratio of 1.4:1 [12].

Epidemiological studies generally found few differences between myeloma cases and controls with respect to previous history of exposure to various infections, allergic or autoimmune disorders, or immunizations [20].

The commonest type of immunoglobulin in our study was IgG, which was found in more than 70 % of patients. Followed by IgA and light chain myeloma, these results were similar to those reported by the Mayo Clinic [14].

Our median overall survival (OS) was 37.5 months (range, 1–84 months) with no significant difference between young and elderly (those over 50 years of age). This could be because most patients were classified as ISS stages I or II and because the variety of treatment modalities is limited. These results are different from those of the SEER study, in which the median survival was 19 months. Being younger (less than 65 years old) was associated with improved OS compared with patients over the age of 75 years (p=0.001) [21]. In our study, we used the cutoff level of 50 years rather than 65 years, as used in the SEER, because of the lower life expectancy in the Egyptian population compared with that of western countries. In a study carried out in Saudi Arabia, the OS was 68 months [15]. A Bulgarian study found no significant difference between in OS between ISS stages II and III [17], although this study involved only 98 patients. Generally, multiple myeloma remains incurable, with most patients experiencing relapse after first-line treatment [11].

The general treatment in our unit is with Endoxan/steroids or Melphalan/steroids. Other lines of treatments including Thalidomide (whether alone or added to previous regimens), VAD regimen or velcade were given to a small number of patients when possible within a clinical trial or by donation. For this reason, the difference in survival was not statistically significant between the lines of treatment.

Treatment with Melphalan/steroids produced different survival in separate studies. Median survival in Chinese patients was reported to be 40 months [9], while in SEER, the median overall survival of patients was 31 months. This could be attributed to ethnic variation. The corresponding median survival for patients treated with all other regimens was 38 months [18]. These data highlight the continuing incurability of multiple myeloma despite all the novel therapies that have improved remission but have still not lengthened OS.

Conclusion

Our records were largely similar to those reported in Chinese studies but different from those of western and even other Arabic countries.

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