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Clinical Profile of Multiple Myeloma in National Oncology Center, Aden, Yemen

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Background: Multiple myeloma (MM) is a malignant disorder characterized by the proliferation of a single clone of plasma cells derived from β-cells in the bone marrow. This present study aims to determine the clinical and laboratory features, stages, and outcomes of newly diagnosed adult myeloma patients and to identify the pattern of multiple myeloma distribution according to gender, age, occupations, risk factors, and geographic distribution.
Materials and Methods: This is a descriptive study of 30 patients diagnosed with multiple myeloma carried out at the Hematology Department of National Oncology Center Aden, Yemen, between 2019 – 2020, with history and physical examination, complete blood count, bone marrow aspiration, serum protein electrophoresis, B2 macroglobulin, albumin, creatinine, and calcium were done for all patients.
Results: Of the 30 diagnosed cases of multiple myeloma, 11 were male, and 19 were female; Male to Female ratio was (1:1.7). The age ranged between 43 – 80 years, where (36.7%) were more than 65 years. The mean age was 63.2 years. Bone marrow plasmacytosis was noted in 100% of cases with a mean count was (32.2%). On serum electrophoresis, M-band was noted in all patients.

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Radio imaging revealed lytic bone lesions in 93.3%. According to ISS: The most common patients presented with stage III (40%). In the study period, (85.6 %) of the patients received bortezomib, cyclophosphamide, thalidomide, and/or lenalidomide with dexamethasone as part of the first-line treatment. The survivors during the research period were (60%) of patients.

Conclusion: This study shows that multiple myeloma is a disease of the middle and elderly aged population with a female preponderance. Bone pain and low backache were the most common presenting symptoms, along with fatigue and weakness. Most patients were in stage III at presentation with severe anemia, lytic lesions, pathological fractures, and renal insufficiency were most observations findings. Bone marrow aspiration, serum electrophoresis, and related investigations play an essential role in diagnosing and managing multiple myeloma cases.

Keywords: Multiple myeloma; plasma cells; bone marrow aspiration; Aden; Yemen.

1. INTRODUCTION

Multiple myeloma is a neoplastic plasma-cell disorder [1] characterized by the proliferation of a single clone of plasma cells that produce a monoclonal protein [2]. The plasma cells' proliferation throughout the bone marrow (BM) leads to extensive skeletal involvement, with an osteolytic lesion, hypercalcemia, anemia, and soft tissue plasmacytoma, excessive monoclonal protein (M protein) production can lead to renal failure and an increased risk of developing life-threatening infections due to the lack of functional immunoglobulins [3,4]. Multiple myeloma represents nearly 1% of neoplastic diseases and 13% of hematologic malignancies, 2% of deaths from all cancer, and 20% of hematological malignancies. The incidence of multiple [5,6] myeloma is lower in the Asian population, and among blacks is twice that in whites. MM is slightly more frequent in men than women, and the incidence increases with age [7]. The cause of MM is unknown. However, many risk factors have been implicated with variable levels of evidence [8,9]. Some variables, such as age, sex, race, and obesity, have a double behavior as risk and prognostic factors. On the other hand, exposure to radiation and certain chemical products such as some herbicides and insecticides has also been demonstrated to be associated with the risk of MM [10]. Myeloma is commonly thought to develop from a monoclonal gammopathy of undetermined clinical significance -usually known as MGUS- that progresses to smoldering myeloma (SMM) and in the latter to symptomatic myeloma by multistep genetic and microenvironmental changes [11,12] . MM is divided into symptoms and non-symptoms according to the lack or presence of myeloma-related organ or tissue dysfunction. Osteolytic bone damage and pressure fractures are the hallmark of the disease and cause considerable morbidity. This increase in bone breakdown can also raise calcium levels in the blood [5]. In multiple myelomas, the overgrowth of plasma cells in bone marrow can crowd out the normal blood-forming cells, leading to low blood counts, which can cause anemia, thrombocytopenia, and leukopenia. Also, the antibody secreted by the myeloma cells does not help the ability to attack a microorganism, leading to recurrent infections. This antibody can harm the kidneys leading to renal damage and even renal failure [13]. Myeloma is usually an incurable disease. In recent years, the introduction of autologous stem cell transplantation and the availability of agents such as thalidomide, lenalidomide, and bortezomib have changed the management of myeloma and extended overall survival [14].

MM diagnosis depends on identifying abnormal monoclonal plasma cells in the bone marrow, M-protein in the serum or urine, osteolytic lesions, and a clinical picture consistent with multiple myeloma. Serum β2-Microglobulin (β2M), albumin, Lactate Dehydrogenase (LDH) in the blood, and specific gene abnormalities (cytogenetics) are the most critical stages and prognostic factors [15]. The standard clinical staging of multiple myeloma back in 1975 when Durie and Salmon developed a Durie-Salmon Staging (DS) system as a prognostic model using the following parameters that predicted myeloma cell tumor burden: Hemoglobin level, serum calcium level, the number of bone lesions on bone X-ray, the level and type of monoclonal protein [16]. Subsequently, Philip Robert Greipp developed an International Staging System (ISS), which uses serum β2-microglobulin and albumin levels and is the most widely adopted multiple myeloma staging system [15]. Recently, the International Myeloma Working Group (IMWG) developed the Revised International Staging System (RISS), which combines elements of tumor burden ISS and disease

biology (presence of high-risk cytogenetic abnormalities or elevated LDH level) [17].

Despite the recent technological advances in the detection of aberrant surface antigens on plasma cells by immunophenotyping, molecular characterization of clonally rearranged immunoglobulin genes, and a spectrum of cytogenetic abnormalities enhanced by FISH, the bone marrow aspirate and trephine biopsy remains the "gold standard" for quantifying the volume of medullary plasma cell infiltration and assessing the degree of plasma cell dysplasia and has prognostic relevance [18,19].

In Yemen, like in many developing countries, where genetic and immunophenotyping are restricted to very few centers, bone marrow aspiration, and serum protein electrophoresis are still crucial in diagnosing multiple myeloma. This study aims to identify typical clinical and laboratory profiles presenting multiple myeloma features.

2. MATERIALS AND METHODS

Thirty patients with multiple myeloma admitted to the Hematology department at National Oncology Center, Aden, South Yemen were studied for the duration of 2019-2020 The data was collected using a convenient sampling method. It was an observational study with the objective to look into the clinical profile of multiple myeloma. All blood examinations, complete blood count, bone marrow aspiration, serum protein electrophoresis, B2 macroglobulin, albumin, creatinine, and calcium were done for all patients. All the new cases of multiple myeloma admitted to the Hematology department at the National Oncology Center were included in the study.

2.1 Statistical Analysis

The employed data collection technique is an open–closed questionnaire covering all necessary variables needed to accomplish the study. The data collected in the questionnaire have been entered into the SPSS program and analyzed in order to find out the frequency, percentage, and mean values with standard deviations, chi-squared test for qualitative, T student test for the difference of two means, and Kruskal Wallis test for the difference of three or more means for quantitive variable, with the 95% confidence limits. A P-Value of ≤ 0.05 was considered statistically significant.

3. RESULTS

The study population consisted of 30 patients with multiple myeloma being studied during a period from between 23rd January 2019 to 23rd December 2020. in National Oncology Center \ Aden.

Table 1 shows that multiple myeloma was more prevalent in female patients, 19 (63.3%), while 11 (36.7%) were in male patients. The M: F ratio was1:1.7. The presenting age of the patients ranged from 43 to 80 years with a mean (of 63.2 ± 8.9 years). Patients age group > 65 were the most common (36.7%) cases.

Table 1. Demographic characteristics of the studied patients with multiple myeloma

Item	(n = 30)	
	No.	**%**
- **Sex:**		
Male	11	36.7
Female	19	63.3
Male : Female ratio	1: 1.7	
- **Age group (years):**		
< 60	9	30.0
60-65	10	33.3
> 65	11	36.7
Mean age (Min.- Max.)	63.2 ± 8.9 (43 - 80)	
Mean age for male patients (Min.- Max.)	63.1 ± 6.8 (49 - 72)	
Mean age for female patients (Min.- Max.)	63.3 ± 10.1 (43 - 80)	

Table 2. Clinical presentation of the studied patients with multiple myeloma by sex

Presentation	Male (n = 11)		Female (n = 19)		Total (n = 30)		p-value
	No.	%	No.	%	No.	%	
Low back pain	10	90.9	16	84.2	26	86.7	0.530
Fatigability	8	72.7	17	89.5	25	83.3	0.245
Shoulder pain	6	54.5	17	89.5	23	76.7	**0.043***
Loss of appetite	6	54.5	16	84.2	22	73.3	0.091
Numbness	8	72.7	13	68.4	21	70.0	0.571
Chest pain	4	36.4	16	84.2	20	66.7	**0.012***
Generalized pain	5	45.5	15	78.9	20	66.7	0.071
Fever	5	45.5	13	68.4	18	60.0	0.197
Muscles weakness	4	36.4	12	63.2	16	53.3	0.150
Headache	5	45.5	10	52.6	15	50.0	0.500
Constipation	6	54.5	9	47.4	15	50.0	0.500
Abdominal pain	4	36.4	9	47.4	13	43.3	0.421
Leg swelling	5	45.5	6	31.6	11	36.7	0.354
Pathological fracture	3	27.3	7	36.8	10	33.3	0.411
Polyuria	1	9.1	6	31.6	7	23.3	0.171
Itching	0	0.0	5	26.3	5	16.7	0.082
Bleeding	0	0.0	2	10.5	2	6.7	0.393
Bruising	0	0.0	2	10.5	2	6.7	0.393
Paraplegia	0	0.0	2	10.5	2	6.7	0.393
Hemiplegia	1	9.1	0	0.0	1	3.3	0.367
Impaired consciousness	1	9.1	0	0.0	1	3.3	0.367

**p-value ≤ 0.05 is statistically significant*

Table 2 shows the most common clinical presentation in patients with MM is low back pain 86% (male, 90.9%, and 84.2% in females), followed by fatigability (83.3%). Shoulder pain shows in (76.7%) with significant statistical difference in sex (p= 0.043), chest pain in (66.7%) with significant statistical difference in sex (p= 0.012).

Table 3 shows that the hematological parameters of patients presented with moderate anemia, mean Hb level was 9.1 ± 2.4 g/dl, range (5.0 - 15.6) with (mean hemoglobin 9.9 ± (3.0) g/dl in males and 8.6 ± (2.0) g/dl in female. There was a significant statistical difference between RBC count and sex (p= 0.048). The mean ESR was more elevated in female than male patients, with 101.9 ± 44.7 mm/hr in females and 82.5± 40.7 mm/hr in males (p=0.253).

Table 4 shows elevated in creatinin (mean =1.6 ±1.2 mg/dl), calcium (mean= 9.3±1.3 mg/dl), B2M (mean= 4.9 ±3.0 µg/ml) and LDH (mean = 300.5±197.6). The only parameter that showed significant difference between male and female was serum LDH (P=0.043).

Table 5 shows that the mean albumin is about (45.0±12.9 g/L) range (20.0- 73.0 g/L), the mean concentration of individual protein fractions α1 (2.8±1.9), α2(8.7±4.1), β1(10.5±6.1), γ-globulin (32.4±14.9) (g/L) respectively.

Table 6 shows free kappa more common in 46% of the patients.

Table 7 shows that bone marrow aspiration was performed in all 30 patients. The hypercellular bone marrow was observed in 43.3% of patients. The erythroid precursors decrease in (73.3%) of patients, 72.7 % in males, and female 73.7%. The percentage of plasma cells ranged from (10-80%) with a mean of 32.2 ± 21.5%.

Table 8 shows that most patients with bone marrow findings represent plasma cells was more than (10-20%) in 40% of patients.

3.1 Survival Analysis

The overall survival during 24 months of follow-up to the studied patients with multiple myeloma showed a mean survival time of 17.8 months (95% CI: 14.4 - 21.1).

Table 3. Hematological parameters by sex of patients with multiple myeloma

Parameter	Male (n = 11)		Female (n = 19)		Total (n = 30)		p-value
	X ± SD	Range	X ± SD	Range	X ± SD	Range	
Hb [g/dl]	9.9 ± 3.0	5.0 - 15.6	8.6 ± 2.0	5.3-13.0	9.1 ± 2.4	5.0 - 15.6	0.170
RBCs [x 10^{12}/L]	3.80 ± 0.93	1.90-5.40	3.02 ±1.03	1.30-5.10	3.30 ± 1.05	1.30- 5.40	**0.048***
MCV [fl]	83.4 ± 5.2	72.4-89.0	84.9 ± 7.9	64.3-96.3	84.3 ± 6.9	64.3- 96.3	0.565
MCH [pg]	26.6 ± 1.9	22.9-29.0	27.7 ± 3.5	20.0-32.9	27.3 ± 3.05	20.0- 32.9	0.390
MCHC [g/dl]	31.6 ± 1.9	27.0-33.0	32.3 ± 2.2	28.0-36.0	32.1 ± 2.1	27.0- 36.0	0.339
WBCs [x 10^9/L]	6.99 ±4.04	1.40-12.6	6.5 ± 2.7	2.30-12.0	6.68 ± 3.2	1.4-12.6	0.693
Neutrophils [%]	59.1 ± 21.8	9.0-85.0	48.2 ± 20.8	12.0-84.0	52.2 ± 21.4	9.0 -85.0	0.185
Eosinophils [%]	0.36 ± 0.62	0-2.0	0.55 ± 0.93	0-3.4	0.48 ± 0.82	0-3.4	0.545
Basophils [%]	0.31 ± 0.16	0-0.8	0.49 ±0.2	0 - 1.8	0.43 ±0.2	0 - 1.8	0.622
Lymphocytes [%]	34.1 ±21.4	10.0 -84.0	38.3 ±20.1	1.9 -78.0	36.7 ±20.3	1.9-84.0	0.601
Monocytes [%]	5.2 ±4.6	0.1 - 12.0	6.53 ±6.42	0.2 -27.0	6.05 ±5.79	0.1-27.0	0.562
Platelets [x 10^9/L]	285.1 ±102.5	121 - 425	236 ±96.1	72 - 498	252.9 ±99.4	72-498	0.213
ESR [mm/hr]	82.5 ±40.7	24 – 140	101.9 ±44.7	15-160	94.5 ±43.5	15-160	0.253

**p-value ≤ 0.05 is statistically significant.*
Hb: hemoglobin concentration
MCV: Mean corpuscular volume
RBCs: Red blood cells count
MCH: Mean corpuscular hemoglobin
MCHC: Mean corpuscular hemoglobin concentration
WBCs: White blood cells count
ESR: erythrocytes sedimentation rate

Table 4. Biochemical parameters by sex of patients with multiple myeloma

Parameter	Male (n = 11)		Female (n = 19)		Total (n = 30)		p-value
	X ± SD	Range	X ± SD	Range	X ± SD	Range	
BUN [mmol/l]	23.5 ±17.7	3 -57	17.7 ±9.6	6-42	19.8 ±13.1	3-57	0.256
Creatinin [mg/dl]	1.9 ±1.7	0.6-6.1	1.4 ±0.9	0.5-4.2	1.6 ±1.2	0.5-6.1	0.336
Albumin [g/dl]	3.5 ±0.9	1.2-4.4	3.4 ±1.1	2.0-6.6	3.5 ±1.05	1.2-6.6	0.863
Calcium [mg/dl]	9.2 ±1.4	7.3-12.7	9.5 ±1.2	7.0-11.6	9.3 ±1.3	7.0-12.7	0.572
LDH [IU/dl]	400.9 ±279	203-129	244.7 ±107.1	102-499	300.5 ±197.6	102-1129	**0.043***
β_2M [µg/ml]	5.1 ±3.1	2.2-10.0	4.8 ±3.0	1.4-10.8	4.9 ±3.0	1.4-10.8	0.837

**p-value ≤ 0.05 is statistically significant.*

BUN: Blood urea nitrogen; LDH: Lactate dehydrogenase; β_2M: Beta 2 microglobulin

Table 5. Plasma protein electrophoresis by sex of patients with multiple myeloma

Parameter	Male (n = 11)		Female (n = 19)		Total (n = 30)		p-value
	X ± SD	Range	X ± SD	Range	X ± SD	Range	
Albumin (g/L)	46.0 ±8.9	35 -59.3	44.4 ±14.9	20-73	45.0 ±12.9	20.0- 73.0	0.763
Alpha-1-Globulin (g/L)	2.9 ±2.1	0.8 - 7.0	2.7 ±1.8	0.8 -8.6	2.8 ±1.9	0.8 -8.6	0.830
Alpha- 2-Globulin (g/L)	9.5 ±4.2	5.3-19.8	8.3 ±4.0	2.3-20.4	8.7 ±4.1	2.3- 20.4	0.428
Beta-1- Globulin (g/L)	10.0 ±6.1	4.2-23.8	10.8 ±6.3	2.5-28.0	10.5 ±6.1	2.5- 28.0	0.729
Gamma Globulin (g/L)	28.7 ±9.9	15- 46	34.6 ±17.0	9.7-68.0	32.4 ±14.9	9.7- 68.0	0.301

p-value > 0.05 is statistically insignificant

Table 6. Free light chains of patients with multiple myeloma

	(n = 30)	
	No.	%
High Kappa free light chain (>19.4 mg/L)	14	46.7
High Lambda free light chain (>26.3 mg/L)	6	20.0

Normal results for kappa free light chains are: 3.3 to 19.4 mg/L

Normal results for lambda free light chains are: 5.71 to 26.3 mg/L

Table 7. Bone marrow findings by sex of patients with multiple myeloma

Findings	Male (n = 11)		Female (n = 19)		Total (n = 30)		p-value
	No.	%	No.	%	No.	%	
- Bone marrow cellularity:							
Normal	3	27.3	4	21.1	7	23.3	0.836
Decreased	4	36.4	6	31.6	10	33.3	
Increased	4	36.4	9	47.4	13	43.3	
- Granulocytic precursors:							
Normal	4	36.4	7	36.8	11	36.7	0.977
Decreased	5	45.5	8	42.1	13	43.3	
Increased	2	18.2	4	21.1	6	20.0	
- Erythroid precursors:							
Normal	1	9.1	3	15.8	4	13.3	0.763
Decreased	8	72.7	14	73.7	22	73.3	
Increased	2	18.2	2	10.5	4	13.3	
- Myeloid to Erythroid ratio:							
Normal	3	27.3	7	36.8	10	33.3	0.808
Decreased	4	36.4	5	26.3	9	30.0	
Increased	4	36.4	7	36.8	11	36.7	
- Megakaryocytes:							
Normal	8	72.7	13	68.4	21	70.0	0.741
Decreased	3	27.3	5	26.3	8	26.7	
Increased	0	0.0	1	5.3	1	3.3	
- Total Lymphoid:							
Normal	5	45.5	8	42.1	13	43.3	0.689
Decreased	1	9.1	4	21.1	5	16.7	
Increased	5	45.5	7	36.8	12	40.0	
Mean plasma cells in BM	**41.1 ± 26.6 (14-80)**		**28.0 ± 18.1 (10-66)**		**32.2 ± 21.5 (10-80)**		**0.119**

p-value > 0.05 is statistically insignificant

Table 8. Percentage of PC infiltrate in Bone Marrow Aspirate

	(n = 30)	
	№	%
Bone marrow plasma cells >10% – 20%	12	40.0
Bone marrow plasma cells 20% –50%	11	36.7
Bone marrow plasma cells >50%	7	23.3

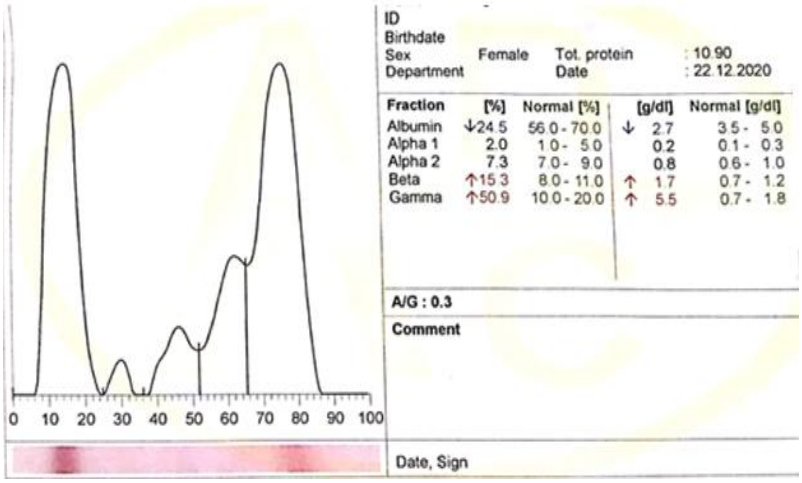
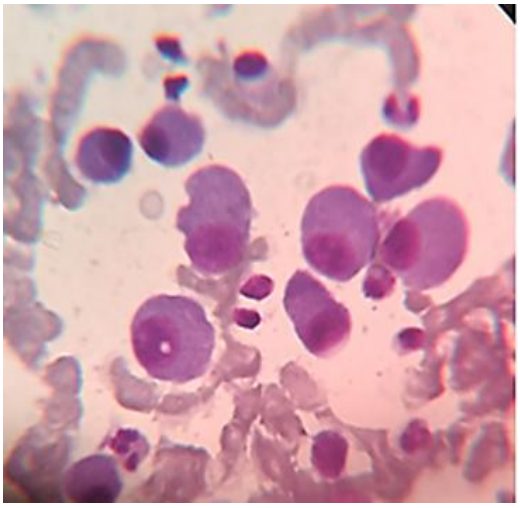
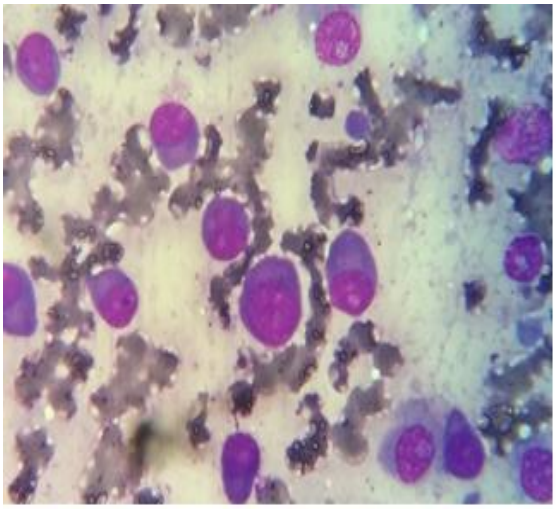


Fig. 1. Serum protein electrophoresis of patient 65 years; Albumin= 24%, Alpha1= 2.0 %, Alpha 2= 7.3%, Beta 1= 15.3%, Gamma Globulin= 50.9 %



Slide 1. Bone marrow aspiration of female 58 years old, showing mature myeloma cells (a round eccentric cartwheel nucleus without nucleoli, abundant basophilic cytoplasm, and a perinuclear hof). (MGGX100, Lishman stain)



Slide 2. Bone marrow aspiration of patient 60 years old showing cluster of plasma blast. (MGGX100, Leishman stain)

4. DISCUSSION

Multiple Myeloma is the third most common after lymphoma and leukemia in southeastern Yemen and were estimated (7%) of hematology malignancy and (1.4%) of all cancer between (2019 – 2020); there was an increase in comparison to studies by Al-Ghazaly, et al. at the hematology Centre in Yemen, between (1999 and 2005) were evaluated 785 of patients more than 14 years old by bone marrow examination and observed the total of multiple myeloma eight present from the total of the patients,[20] while in Abdul-Hamid study in Al-Gamhouria teaching hospital in Aden, between (2008-2010) the total 300 patients aged between18-80 years showed that 12 (4.0%) patients had MM [21]. To date, in NCI SEER Program (National Cancer Institute and Surveillance, Epidemiology and End Results), myeloma represented 1.8% of all new cancer cases in the U.S [22]. In 2021, it was estimated that there would be 34,920 new cases of myeloma. The rate of new cases of myeloma was 7.1 per 100,000 for both genders per year; these rates are age-adjusted and based on 2014–2018 [23].

In this study, females (63.3%) were more affected than males (36.7%) with M: F ratio was 1:1.7. These results are similar to a study in Benghazi (Libya), were observed females (57.6%) were more affected than male (42.4%) [24]. In contrast with studies in United Arab Emirates, North East India, and China, the rates were higher in males compared with females for prevalence [25-27]. In another study in (India), both genders showed equal affection [28].

The ages of patients in this study ranged from 43 to 80 years with a mean of 63.2 ± 8.9 years; this similar study in South India recorded the mean age group as 64 ± 10.77 years. The mean age of patients was 52, 56, 57, and 60 years in other studies by Chowdhury et al. (Bangladesh) [29] Sultan, et al. (Pakistan) [30] Pegu, et al. (India), [31] and Abdul-Hamid in (Aden\Yemen) respectively [21].

The diagnosis of symptomatic MM requires the presence of an M-protein in serum and/or in urine, increasing plasma cells in the bone marrow or plasmacytoma, and related organ or tissue impairment (including bone lesions) [30]. The most common present symptoms in this study were bony pain which included low back pain (86.7%), shoulder pain (76.7%), chest and generalized pain (66.7%), in some patients were associated with a pathological fracture (33.3%), fatigue was other presenting symptoms in (83.3%) of the patients result from anemia, this is results similar to other studies, in Senegal by Fall, et al. were the bone pain observed in (96.3%), Kumar et al., a study in the northeast (India) patients presented with backache and other bone pains in (86%), generalized weakness and easy fatigability in (80%) and pathological fracture (48%),[25] also in Diwan, et al. study (India) recorded bony pain in (85%) the common symptoms presented in the patients, [28] while in Pakistan study observed fatigue (81.9%) the most common presented follow by backache (80.3%) and bone pain (67.2%) [26]. Cancer anorexia-cachexia syndrome (CACS) is a devastating and debilitating aspect at any stage of malignancy. It primarily presents anorexia, weight loss, and muscle wasting secondary to inadequate oral intake and metabolic changes. This syndrome is highly prevalent among cancer patients, significantly impacts morbidity and mortality, and impinges on patient quality of life. The pathogenic mechanisms of CACS are multifactorial. It is suggested to be the result of tumor-host interactions, and cytokines have a significant role. Loss of appetite (anorexia) was observed in this study in (73.3%) of patients, and this complaint was also found in a study by Hawkins; this study aimed to prove that anorexia present in patients with advanced malignancy and can be a source of considerable distress, were recorded the anorexia (79%) among 115 of patients [32].

The hematology parameter in this study showed that most patients had low mean hemoglobin levels and lymphocytosis, and half of the patients had normal leucocytes and platelet counts.

In laboratory studies, anemia was present in most cases; it ranged from average to severe degrees. The reason for anemia in MM can be either a result of renal impairment or can be due to bone marrow failure because of marrow infiltration by myeloma cells. In the present study, most of the patients presented with anemia observed (93.3); the highest percentages present with moderate anemia (43.3%) (Hb: <11.0 – 8.0 g/dL), male (36.4%), and (47.4%) in female, compared to other studies, also the most patients present during the diagnosis with Anemia were found in Benghazi, and South India studies the anemia (Hb <10 gm/dl) in (50.5%) of cases, in Saudi Arabia anemia was found at the time of diagnosis in (74%) [24,33,34]. The mean total leukocyte count was (6.68 ± 3.2%), leucocytosis was found in (16.7%), leukopenia (WBC < 4.0) was in (23.3%), the other patients (60.0%) with a typical range (4.0 – 10.0) in comparison to Kaur's study leukopenia in (7.2%), leukocytosis (35.7%) and (57.1%) were in the normal range approximately similar to this study [35]. Thrombocytopenia, in general, may be due to infiltration of the marrow by plasma cells or intravascular destruction of platelets, or thrombopoietin activity of IL-6 [36]; in this study, thrombocytopenia was (26.7%) this similar to a study in Pakistan (2006 -2018), and other studies in India have observed thrombocytopenia in (27.5%) and (25%) respectively [33,37].

The erythrocyte sedimentation rate (ESR) was elevated significantly in multiple myeloma, often used as an indicator of active disease, although this test is considered nonspecific [38]. In this study, ESR was elevated in (70.0%) of patients, nearly similar to a study by Sunil Jagtap, where ESR was elevated in (66.7%), and in Azhar Hussain's study [23,24,39], while in Kiran Amir study was elevated in (91%) of the patients [40].

Renal failure remains a principal cause of morbidity for patients with multiple myeloma.

Once reversible factors such as hypercalcemia have been corrected, the most common cause of severe renal failure in these patients is an interstitial tubule pathology that results from the very high circulating concentrations of monoclonal immunoglobulin free light chains [41]. In the current study, raised serum creatinine of more than 2 mg/dl was found in (30.0%) of the patients, which is similar to findings in the study of Hesham et al., where was renal dysfunction observed in (38%) and in the study of Salem, et al. observed in (18.5%) [42,43]. Hypercalcemia was observed in this study (26.7%) of patients, and it is similar to other studies, where hypercalcemia was found in a study in Saudi Arabia in (19.6%) of patients [2,29,43].

Serum β2-microglobulin and albumin are the two most important prognostic factors. Hypoalbuminemia (serum albumin less than 3.4 g/dL) was present in half of the patients, about 53.3 %; this is similar in other studies [29,44]. In the present study, the mean serum of β2-microglobulin (4.9±3.0) raised in 73.3% of the patients; this is similar to a study in the United States (Minnesota), the β2-microglobulin level was increased in 75% [45], and India, (Punjab) study was increased in (71.4%) [36].

The mean serum of lactate dehydrogenase in this study was (300.5±197.6); compared with a study by Azhar Hussain, the mean level of LDH was (438±253) [46]. In this study, 20 % of patients' LDH is more than 480 IU/dl, and 40% of both < 240 IU/dl and between 240 – 480 IU/dl; this is similar to other studies [25,29,36].

In this study, serum protein electrophoresis revealed a localized band in all patients as(100%); this is similar to Diwan AG studies (India) showed monoclonal protein in all cases (100%), and Shifa studies (Pakistan) (97.5%) of cases [28,47]. While in Khalil's study (Riyadh), serum protein electrophoresis showed a monoclonal paraprotein in (78%) of the cases [43].The mean concentration of individual protein fractions α1(2.8±1.9), α2(8.7±4.1), β1(10.5±6.1), γ-globulin(32.4±14.9) (g/L) respectively. These results are within the range of reported studies such as Azhar Hussain (Libya); the mean concentration of individual protein fractions α1, α2, β1, and γ-globulin was 4.66±1.88, 10.2±3.7, 9.4±13.5, 23.1±16.7 (gm/dL) respectively [23].

Serum free light-chain assay is recently approved for diagnosing multiple myeloma patients. This study aimed to evaluate the value of sFLC ratio at baseline in newly diagnosed multiple myeloma, increased free kappa chain of more than 19.4 mg/L observed in (46.7%) and free lambda chain of more than 26.3 mg/L in (20.0%) of the patients, comparing to a study in Egypt were observed 70 % of patients have kappa chain-positive [48].

The presence of Bence Jones proteinuria significantly raises suspicion for multiple myeloma and warrants referral to a hematology clinic. In this study BJP for urine test was positive in (23.3%) of the patient and negative in (76.7%); comparing to other studies, in Saudi Arabia's study, urine Bence Jones protein was positive in (35.7%) [43], in Brazil's study (52.6%) that presented was negative and positive in (47.4%) [49], while in Qatar's study (74.7%) was reported as positive [42].

A blood smear examination showed that the anemia was normocytic normochromic noted in the majority of patients (53.3%), and microcytic hypochromic (26%), while comparable to an Indian study, was observed normocytic anemia in (85%) of the patients [18]. Red cell morphology was mild and abnormal, with exaggerated variation in cell size and occasional anisocytosis. Rouleaux formation was observed in (80.0%), similar to a Ludhiana (India) study by Puneet Kaur [36].

According to the international staging system (based on serum β2 macroglobulin and serum albumin) in this study, most of the patients who presented in the late stage were observed stage III (40.0%) followed by stage II (33.3%) and stage I (26.7%) this is similar to Sultan studies (Pakistan from 2012 to 2015) stage III was (46.1%) were in stage II was (30.7%) and stage I (23%) [33]. Compared to a study by Fadi Nasr (Lebanon), stage III was (50.8%) stage I in (25.4%), and stage II was (23.8%) [50], while in the United Arab Emirates study by Arif Alam, and other studies stage II was the most common followed by stage 3 and stage I [24,51,42].

In this study, the clinical outcome during the study period was death (40%) and still alive (60%). When comparing the overall cancer death rate in Cancer Center (Aden) with the death rate of myeloma, it was found that it constituted 15% of the total cancer deaths (2019-2020); this is nearly similar to a study in Saudi Arabia it is estimated that MM and lymphomas accounted for (9.6%–11%) of cancer-related deaths in the Kingdom in 2014 [52]. In the United States,

myeloma is the fifteenth leading cause of cancer death; the death rate was 3.2 per 100,000 men and women per year based on 2015–2019 deaths, age-adjusted.

The clinical outcomes period stratified by ISS staging of patients with multiple myeloma during the study showed that more common in stage I was still alive (75.0%) followed by stage II (70.0%), but in stage III was only (41.7%), and the overall survival about this stages slightly higher mean survival time among stage I patients 19.6 months when compared to stage II patients 18.9 months and stage III patients 15.6 months; he is similar to study in Brazil (2012) after 5 years of follow-up, the estimated OS for Stages I, II and III is 68.2%, 52.7%, and 30.4% respectively, while different in median OS were found 62 months of stage I, 49 to 65.5 months for Stage II and 26 to 29 months for Stage III.

The survival of patients with multiple myeloma (MM) has significantly improved over the last two decades with the broader use of novel drugs and autologous tandem transplantation.

The overall survival during 24 months of follow-up for the studied patients with multiple myeloma showed a mean survival time of 17.8 months; in a study at the Kasr Al Aini Hospital between 2000 and 2010 by Noha, El Husseiny mean overall survival was 37.5 months (range from1-84 months) [49].

5. CONCLUSIONS

Multiple Myeloma was more common in females than males (M: F= 1:1.7). The peak age for multiple myeloma in this study was more than 65 years (36.7%), followed by ages between 60-65 years (33.3%) and (30.0%) less than 60 years old. The most common clinical presentation in patients of MM is low back pain (86%) followed by fatigability (83.3%) with shows statistical differences with sex in shoulder pain ($p= 0.043$), chest pain ($p= 0.012$), and infection ($p = 0.041$). ESR was raised in (70.0%) of patients, and rouleaux formation, the most common finding, was observed in the peripheral smear in (80.0%) of patients. Most of the patients presented with $\beta2M \geq 3$ µg/ml in (73.3%) and serum albumin less than 3.4 g/dL in (53.3%). The clinical outcomes during the study were still alive in 60% and death in (40%), and this is more common in males (45.5%) than females (36.8%). Death during the study, according to ISS, was higher in stage III (58.3%). The survival for 24 months of follow-up for the studied patients with multiple myeloma showed a mean survival time of 17.8 months.

CONSENT

Written consent was obtained from adult patients. Patients were informed about the study's aim, which is essential and beneficial for them and their treatment use. Patients are not obliged to enter this study; any patient disagreed with would not be intended.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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