Retrospective Analysis of Presentation, Treatment, and Outcomes of Multiple Myeloma at a Large Public Referral Hospital in Eldoret, Kenya

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PURPOSE
Treatment patterns and survival outcomes of patients with multiple myeloma (MM) in Kenya have not been adequately characterized. The objectives of this study were to describe the clinical, laboratory, and imaging findings at diagnosis, to describe the treatment offered, and to determine the survival outcomes of patients with MM over an 11-year period.

PATIENTS AND METHODS
A retrospective chart review was carried out for all patients who were diagnosed and treated for MM at Moi Teaching and Referral Hospital from 2009 to 2019. The Kaplan-Meier method was used to estimate survival. Factors affecting survival were identified using univariate and multivariate analyses.

RESULTS
A total of 221 patient charts were analyzed of which 124 belonged to male patients (56.1%). The median age at diagnosis was 61 years. Bone pain was the most common presenting complaint observed in 69.6% of 194 patients assessed. Out of 102 patients who received imaging studies, 60 (58.8%) had lytic lesions, 30 (29.4%) had fractures, whereas 30 (29.4%) had spinal cord compression. Anemia, renal failure, and hypercalcemia were observed in 87/187 (46.5%), 22/161 (13.7%), and 23/42 (54.8%) patients, respectively. Thalidomide and dexamethasone (65.2%); bortezomib, thalidomide, and dexamethasone (14.6%); and melphalan and prednisolone (11.9%) were the most prescribed initial chemotherapy regimens among 219 patients analyzed. Overall survival at 1 and 5 years was 70% and 21%, respectively; median overall survival was 29.0 months. In multivariate analysis, male sex (hazard ratio [HR] 1.9), baseline anemia (HR 1.8), and baseline renal failure (HR 3.2) were associated with significantly shorter survival.

CONCLUSION
Survival outcomes were poor despite increased use of multiagent-based chemotherapy regimens. Greater access to available diagnostics and treatments is required to achieve rational treatment and increased survival.

INTRODUCTION
Multiple myeloma (MM) is a hematologic malignancy characterized by ≥ 10% clonal plasma cells in the bone marrow or biopsy-proven bony or extramedullary plasmacytoma with a myeloma-defining event: hypercalcemia, renal failure, anemia, or bone lesions; or any biomarker of malignancy such as clonal plasma cells ≥ 60%, a serum-free light chain (FLC) ratio of ≥ 100, or > 1 focal lesion on magnetic resonance imaging. It is commonly diagnosed among persons between 65 and 74 years of age and has a male preponderance. Six hundred seven new MM cases and 501 MM deaths were reported in Kenya in the year 2018, corresponding to 1.3% of new cancer cases and 1.5% of cancer deaths, respectively.

Although incurable, MM responds to treatment. Patients treated with bortezomib, lenalidomide, and dexamethasone (VRD) followed by autologous stem-cell transplantation and subsequent maintenance with lenalidomide and dexamethasone can achieve a median overall survival (OS) of 75 months. For transplant-ineligible patients, continuous VRD therapy has been shown to have an encouraging median OS of 71 months. Other agents used in the treatment of MM include thalidomide, prednisolone, cyclophosphamide, and melphalan. Despite development of national guidelines for diagnosis and treatment of MM in Kenya, patients are often not able to receive stem-cell transplantation, and access to novel agents such as bortezomib and lenalidomide is limited. Little research has been conducted on MM in sub-Saharan Africa and Kenya in particular. Although characterization of presenting features has been done, treatment and survival have not been adequately described. The objectives of this study were to describe the clinical, imaging, and laboratory findings...
at diagnosis, to describe the current treatments offered, and to determine survival outcomes in a cohort of patients with MM from Western Kenya.

**PATIENTS AND METHODS**

**Study Design and Setting**

We performed a retrospective chart review of MM cases diagnosed and treated at the Academic Model Providing Access To Healthcare—AMPATH Oncology, a collaborative effort of Moi Teaching and Referral Hospital (MTRH), Moi University School of Medicine, and a consortium of North American Institutions led by Indiana University. MTRH is the second largest public hospital in Kenya serving residents of Western Kenya Region, a population of approximately 24 million.

**Patients**

Clinical records of patients who met the diagnostic criteria of active MM according to the International Myeloma Working Group (IMWG) were included. Only patients who were diagnosed and treated between January 1, 2009, and December 31, 2019, were included.

**Data Collection**

A data form was used to collect required data from the electronic health records and files of individual patients. Demographic data including age at diagnosis, sex, and diagnosis date were collected. Presenting signs, symptoms, Eastern Cooperative Oncology Group (ECOG) performance status, radiographic findings, and laboratory findings at diagnosis including full hemogram, renal function tests, serum protein electrophoresis, serum FLC, bone marrow plasma cell percentage, and β2 microglobulin were recorded as well. Initial chemotherapy regimens prescribed, remission status, and date of death or date of last contact were also collected. Data from laboratory and imaging tests were collected up to 3 months after diagnosis because a considerable number of patients could not obtain funds to have a full diagnostic work-up done at the exact moment of diagnosis.

**Outcome Measurement**

Clinical staging was determined using the International Staging System. Remission was considered to have occurred if a serum M protein of 0 g/dL was recorded for a patient who had elevated levels at diagnosis.

**Statistical Analysis**

Based on the sample size calculation for proportions with a finite population correction, assuming a 50% OS at 1 year post-diagnosis, a precision of 5%, and a 95% confidence level, the minimum sample size required was 141. The Kaplan-Meier method was used to determine the median OS and survival rate at 1 year and 5 years after diagnosis. Death of a patient was considered an event. Patients who had not died at the end of the study period and patients lost to follow-up were censored. Univariate survival analysis was carried out using logrank tests for known and hypothesized prognostic indicators including sex, age at diagnosis, ECOG performance status; baseline levels of hemoglobin, platelet count, serum creatinine, calcium, albumin, bone marrow plasma cell percentage; initial chemotherapy regimen; and remission status. A multivariate Cox-regression model was then built using a stepwise selection approach with P ≤ .05 as entry criterion and P ≥ .1 as removal criterion. A two-sided P < .05 was required to achieve statistical significance. Data management was carried out using Stata Version 13, R, and Microsoft Excel.

**Ethical Issues**

Ethical approval (FAN: 003619) was obtained from the Institutional Research Ethics Committee of MTRH.

**RESULTS**

Table 1 is a summary of demographic, clinical, and treatment characteristics of study patients. A total of 221
patients, of whom 124 were males (56.1%), were analyzed. Out of 220 patients assessed, 74.5% were between 50 and 74 years of age, 15.5% were < 50 years of age, and 10.0% were ≥ 75 years of age at diagnosis. The median age was 61 years. Out of 97 patients evaluated, a majority (80.4%) were in ECOG performance status 2 or better, at diagnosis.

| TABLE 1. Demographic, Clinical, and Treatment Characteristics of Study Patients |
|---------------------------------|-----------------|-----------------|-----------------|
| Characteristic                  | No.             | Male            | Female          |
| Sex                             | 221             | 124 (56.1)      | 97 (43.9)       |
| Age, years                      | 220             |                 |                 |
| < 50                            | 34 (15.5)       |                 |                 |
| 50-64                           | 107 (48.6)      |                 |                 |
| 65-74                           | 57 (25.9)       |                 |                 |
| ≥ 75                            | 22 (10.0)       |                 |                 |
| ECOG performance status         | 97              |                 |                 |
| 0                               | 20 (20.6)       |                 |                 |
| 1                               | 35 (36.1)       |                 |                 |
| 2                               | 23 (23.7)       |                 |                 |
| 3                               | 14 (14.4)       |                 |                 |
| 4                               | 5 (5.2)         |                 |                 |
| Presenting clinical features at diagnosis | 194 | Bone pain 135 (69.6) |                 |
| Generalized body weakness 38 (19.6) |                 |                 |
| Numbness 13 (6.7) |                 |                 |
| Fatigue 9 (4.6) |                 |                 |
| Bleeding 4 (2.1) |                 |                 |
| Imaging findings               | 102             |                 |                 |
| Lytic lesions 60 (58.8)         |                 |                 |
| Fractures 30 (29.4)             |                 |                 |
| Cord compression 30 (29.4)      |                 |                 |
| Laboratory Parameters (reference ranges) | No. | Median (range) | Category No. (%) |
| Hemoglobin (11.5-16.5 g/dL) 187 | 10.3 (4.1-15.6) | < 10 | 87 (46.5) |
| Platelets (150-450 × 10^9/mm³) 187 | 247 (14-1,137) | < 150 | 31 (16.6) |
| WBC (4-11 × 10^9/mm³) 189 | 6.3 (2.8-36.5) | < 4 | 24 (12.7) |
| Neutrophils (2-7 × 10^9/mm³) 135 | 4.65 (1.1-83.4) | < 2 | 18 (13.3) |
| Creatinine (75-155 μmol/L) 161 | 75 (1.1-913.9) | ≥ 177 | 22 (13.7) |
| Total calcium (corrected) (2.1-2.6 mmol/L) 42 | 2.6 (1.1-12.2) | > 2.6 | 23 (54.8) |
| Total protein (64-83 g/L) 91 | 86.0 (0-158) | > 83 | 48 (52.7) |
| Albumin (35-50 g/L) 128 | 30.1 (4-61.8) | < 35 | 82 (64.1) |
| Monoclonal protein (0 g/L) 115 | 61 (0-166) | > 0 | 103 (89.6) |
| FLC (κ:λ) ratio (≥ 0.26 to ≤ 1.65) 21 | 63.6 (0.01-3,500) | < 0.26 | 2 (9.5) |
| Bone marrow plasma cell (< 10%) 107 | 50 (2-95) | ≥ 10 | 91 (85.0) |
| β2 microglobulin (< 3.5 mg/L) 13 | 3.3 (2-105) | ≥ 5.5 | 4 (31) |
| Initial Chemotherapy Regimen (N = 219) | No. | Regimen No. (%) |
| T (D) 143 (65.2) |                 |
| VTD 32 (14.6) |                 |
| MP 26 (11.9) |                 |
| Others 18 (8.2) |                 |

NOTE. Other initial chemotherapy regimens prescribed included bortezomib/melphalan/prednisolone (VMP), bortezomib/lenalidomide/dexamethasone (VRD), bortezomib/cyclophosphamide/dexamethasone (VCD), lenalidomide/dexamethasone (RD), and bortezomib/dexamethasone (VD).

Abbreviations: ECOG, Eastern Cooperative Oncology Group; FLC, free light chain; MP, melphalan/prednisolone; TD, thalidomide/dexamethasone; VTD, bortezomib/thalidomide/dexamethasone.
Presenting Clinical Features at Diagnosis

Bone pain was present in 135 out of 194 patients assessed (69.6%). Common locations for bone pain included the back (43/135, 31.9%), limbs (33/135, 24.4%), chest (29/135, 21.5%), and pelvis (12/135, 8.9%). Other features reported included generalized body weakness, numbness, fatigue, and bleeding (Table 1).

Imaging Findings at Diagnosis

Out of 194 patients analyzed, 102 (52.6%) had at least one imaging study done at diagnosis using either x-ray (42/102, 41.2%), magnetic resonance imaging (40/102, 39.2%), or computed tomography (38/102, 37.3%). Lytic lesions were detected in 60 out of 102 patients (58.8%) who received imaging. Common locations for lytic lesions included the spinal column (30%, n = 18), pelvic skeleton (12%, n = 7), and skull (8%, n = 5). Twenty-nine percent of patients (30/102) had fractures. Of these, 23 patients (77%) had vertebral compression fractures. Spinal cord compression was observed in 29.4% of 102 patients who received imaging studies.

Laboratory Findings at Diagnosis

The following abnormal laboratory parameters were frequent: anemia—hemoglobin < 10 g/dL (87/187, 46.5%); hypercalcemia—total corrected calcium > 2.6 mmol/L (23/42, 54.8%); hyperproteinemia—total protein > 83 g/L (48/91, 52.7%); and hypoalbuminemia—albumin < 35 g/L (82/128, 64.1%). The occurrences of elevated monoclonal protein (103/115, 89.6%) and bone marrow plasma cell percentage > 10% (91/107, 85%) were very high (Table 1). International Staging System stage could only be determined for 11 patients; three patients were in stage I and four patients were in stage II and stage III each.

Chemotherapy and Response

Out of 219 patients evaluated, 218 received chemotherapy, whereas one declined treatment. The most prescribed initial chemotherapy regimen was thalidomide and dexamethasone (TD; 65.2%, n = 143) followed by bortezomib, thalidomide and dexamethasone (14.6%, n = 32); and melphalan and prednisolone (MP; 11.9%, n = 26; Table 1). Other regimens prescribed included bortezomib, melphalan, and prednisolone; VRD; bortezomib, cyclophosphamide and dexamethasone; lenalidomide and dexamethasone; and bortezomib and dexamethasone. Bortezomib was prescribed to 46 patients (21.0%), whereas lenalidomide was prescribed to seven patients (3.2%) as part of initial regimens.

Most patients prescribed for TD or MP received 10 cycles or more. Therapy was stopped or changed because of toxicity or treatment failure. For patients receiving bortezomib, thalidomide, and dexamethasone or other triple regimens, six cycles were administered to majority of the patients. More cycles could not be offered because of high drug costs. Maintenance therapy was not routinely offered to any patient group for the same reason. Instead, upon completion of the initial course of treatment, most patients were put on treatment holiday until clinical relapse or until re-emergence of serum M protein, and in patients with baseline and repeat values available, when chemotherapy would be reinitiated. Suboptimal adherence was common because of drug supply interruptions at the study site.

All patients received adjunctive bisphosphonate treatment, and aspirin was prescribed to all patients receiving immunomodulatory agents, unless contraindicated.

Among 103 patients with elevated levels of serum M protein at diagnosis, 44 (42.7%) achieved remission (serum M protein of 0 g/dL). Systematic assessment of response according to IMWG criteria14 could not be carried out because of high costs of monitoring tests.

Survival

Of the 221 patients included in survival analysis, 13 (5.9%) were lost to follow-up and 102 died (46.2%). The 1-year and 5-year survival rates were 70% and 21%, respectively. After a median follow-up of 11.8 months, the median OS was 29.0 months, 95% CI 20.1 to 40.2 months (Fig 1). In univariate analysis, male sex, baseline anemia (hemoglobin < 10 g/dL), thrombocytopenia (platelets < 130 x 10⁹/L), renal failure (serum creatinine > 177 μmol/L), hypalbuminemia (albumin < 35 g/L), and not achieving remission were associated with shorter survival (Figs 1-4), whereas age at diagnosis, ECOG performance status, baseline serum calcium, and bone marrow plasma cell percentage were not associated with length of survival. There were no differences in survival among patients who received different types of initial chemotherapy regimens. In multivariable Cox regression analysis, only male sex (hazard ratio [HR] 1.9, 95% CI 1.1 to 3.3), hemoglobin < 10 g/dL (HR 1.8, 95% CI 1.1 to 3.0), and serum creatinine > 177 μmol/L (HR 3.2, 95% CI 1.7 to 5.8) were associated with an adverse survival outcome.

DISCUSSION

MM was predominantly diagnosed among persons in their sixth and seventh decades of life. The median age at diagnosis reported in this and other sub-Saharan Africa studies ranging from 53 to 62 years was closer to that reported for the African American population (65 years) and lower than that reported for White patients (71 years).10,11,15-17 It appears that sub-Saharan Africans are at risk of early onset MM, a characteristic that has been confirmed in the African American population.17

Bone pain was the most recognizable presenting complaint affecting more than 70% of patients with MM in this and previous research.16,18,19 Studies from Burkina Faso and Ghana reported a high prevalence of back pain as was observed in the current study.10,20 Other symptoms reported including weakness, fatigue, and bleeding could be because of anemia and thrombocytopenia, which are not

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Peripheral neuropathy was infrequently reported in line with findings from a study done in Sudan. Only about half of the patients evaluated received baseline imaging tests, which should form part of the standard work-up for all patients with MM. Baseline imaging may assist the clinician to detect occult lesions and therefore initiate prompt treatment. Evidence of bony progression can also be readily observed by comparing baseline and follow-up imaging. The high cost of imaging studies could have contributed to the low imaging prevalence observed as clinicians requested for imaging studies only in the presence of a compelling indication such as suspected fracture or spinal cord compression. The occurrence of lytic lesions observed at diagnosis at 58.8% was similar to what has been reported in previous research ranging from 50% to 80%. In one Ghanaian study where 80% of participants were evaluated for lytic lesions, a high occurrence of 76.1% was reported. It is therefore possible that the

![Chart A](image1)

**FIG 1.** (A) OS for all patients and (B) OS by sex. NA, not attained; OS, overall survival.

![Chart B](image2)

**FIG 2.** (A) OS by baseline hemoglobin level and (B) by baseline platelet count. NA, not attained; OS, overall survival.
occurrence of lytic lesions may have been underreported in this study. The common sites for lytic lesions (vertebral column and skull) reported in one study were also prevalent in this study.10

Severe bony events represented by fractures particularly to the spinal column were prevalent corroborating reports from Kenya and Cameroon.11,23 Spinal cord compression, an oncologic emergency needing immediate attention, was detected in a considerable proportion of patients (29.4%), which was comparable to what was reported in a Senegalese study (16.9%) and a Cameroonian study (46.8%).18,23

Anemia (Hb < 10 g/dL) prevalence was high in our study with approximately half of the patients being affected. Studies by Othieno-Abinya et al and Kiraka et al both from Kenya reported similar occurrence of anemia,11,15 whereas a study from Ghana reported a higher occurrence at 75%.10 Other studies have reported different degrees of anemia with prevalence ranging from 30% to 83%.10,16,18,19,23 Although anemia is a highly sensitive feature in MM, which presents an opportunity for diagnosis, it could lead to misdiagnosis if not properly investigated because of its poor specificity. It is because of this central role that anemia can play in the diagnosis process that prospective studies are needed to confirm its prevalence in sub-Saharan African populations.

A few of our patients presented with renal failure. Renal damage is multifactorial and may also arise from hypertension, anemia, amyloidosis, urinary tract infections, hypercalcemia, and nephrotoxic nonsteroidal anti-inflammatory drugs. Different degrees of renal dysfunction have been observed in 7%-52% of patients evaluated in studies across sub-Saharan Africa.10,11,16,18,19,24

Hypercalcemia was frequently reported affecting more than half of the patients. A Senegalese study found similar levels of hypercalcemia.18 By contrast, studies from Kenya and Ghana found lower occurrence at around 35%.10,11 A selection bias could explain the high occurrence observed because clinicians only requested for a calcium test when hypercalcemia was suspected potentially excluding patients with normal calcium levels from the evaluated sample.

The characteristic monoclonal protein in MM was demonstrable in a majority of patients consistent with previous findings.10,11,20,25 However, accompanying serum FLC readings for most patients in whom serum M protein was not detected could not be found precluding proper characterization of this special group. Also found in a majority of patients was bone marrow plasmacytosis, which has been reported to be equally high in other studies.10,15,18,20,23

A high proportion of patients had a low albumin level suggestive of poor prognosis.12 Extremes of serum FLC ratio, which is also a poor prognostic indicator,26 was prevalent, albeit few patients were evaluated. β2 microglobulin testing, and hence staging, was not done on most patients because of its high cost.

Access to thalidomide or bortezomib as part of initial chemotherapy regimens was relatively high, which is similar to findings of a survey of hematologist prescribing patterns in Nigeria.27 Reports from Ghana and Senegal

FIG 3. (A) OS by baseline serum creatinine and (B) by baseline serum albumin. NA, not attained; OS, overall survival.
Several features of advanced disease including anemia, renal failure, and hypoalbuminemia were linked to poor survival similar to past studies.\textsuperscript{10,18,24} Notably, age at diagnosis, which is a known prognostic factor, was not found to be associated with length of survival, echoing the findings of Acquah et al.\textsuperscript{10} Additionally, male sex was associated with poor survival, a finding that although infrequent has been reported by Costa et al.\textsuperscript{29} The effects of age and sex on survival may have been modified by other prognostic factors that could not be accounted for such as comorbid conditions and clinical stage.\textsuperscript{30} Furthermore, income levels and insurance coverage may have influenced patients’ ability to acquire treatment thereby indirectly affecting survival.\textsuperscript{29} The known survival benefits of bortezomib-based triple regimens, which are now considered standard treatment,\textsuperscript{31} could not be demonstrated partly because of the small proportion of patients who received these regimens.

Despite limited testing, patients found to have responded to treatment appeared to have a survival advantage, underscoring the need for regular response monitoring to facilitate prognostication and inform appropriate changes in treatment.

This study reveals the survival pattern of patients receiving thalidomide-based regimens, which has not been addressed by previous research from sub-Saharan African cancer centers. A complete picture of how patients presented and the effect of treatment intensity on survival could however not be obtained because of missing data. Future research efforts should be directed toward prospectively determining the depth of response and survival of patients receiving bortezomib-based triple regimens that are increasingly being adopted as initial treatment options. Establishing the effect of socioeconomic factors on outcomes should also be a research priority because of the prolonged and costly nature of MM treatment.

In conclusion, although MM features of bone pain, anemia, renal failure, and hypercalcemia were readily observed, a considerable number of patients did not receive baseline imaging tests, staging tests, and tests required for monitoring of disease progression and treatment. Survival outcomes were modest despite increased use of chemotherapy regimens containing thalidomide and bortezomib. Improved access to proper staging and routine use of available combination chemotherapy are needed to increase survival of patients with MM in Kenya.
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