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# Epidemiological, clinical and biological aspects of multiple myeloma at the Mohammed VI University Hospital in Marrakech

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## ABSTRACT

***Introduction**: Multiple myeloma (MM) is a clonal proliferation of plasma cells invading the bone marrow and secreting a monoclonal immunoglobulin. MM is the second most common haemopathy after non-Hodgkin's lymphoma. **Objective**: The aim of this study is to study the epidemiological, clinical and biological features of multiple myeloma in the population of Marrakech and regions. **METHODS**: Through a retrospective descriptive study spread over 3 years, concerning 92 cases of patients followed for MM. Included in the study are any patient with radiological, biological, cytological or histological criteria for MM. **RESULTS**: The mean age of the patients was 59.5 years and the sex ratio (m / f) was 1.3. Growers account for 13%, 10 patients are tobacco, and 2 are alcoholics. 12 patients have diabetes, 8 are hypertensive, 2 are treated with TB. Clinically, 85.9% of bone manifestations, 42.4% of anemic syndromes, 46.8% of altered general status and 35% of neurological symptoms were noted. Biological examinations showed anemia with hemoglobin of less than 10 g / dl in 64% of cases, accelerated SV in 70.6%, an increase in serum creatinine in 34.7%, and hypercalcemia In 22.8%. A monoclonal peak in serum protein electrophoresis was noted in 88% of which Ig G (64%), IgA (25%), light chains (8.3%), hypogammaglobulinemia in 5.4%. Cytologically, the myelogram revealed a medullary plasmocytosis greater than 10% in 91.3% cases with dystrophic aspects. According to the classification of Salmon and Durie, 65% of patients were stage III, 22% stage II, and 13% stage I. **CONCLUSION**: MM is a hemopathy that remains incurable and often fatal, however diagnosis and management Remain due to the ignorance of this disease and the remoteness of the sick.*

**Keywords** : Multiple myeloma, gammapathy, plasmocytosis.

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## INTRODUCTION

Multiple myeloma or kahler disease is defined by malignant proliferation of a plasma cell clone in the bone marrow often producing a monoclonal immunoglobulin [1]. It is a rare disease that accounts for about 80% of malignant monoclonal gammopathies and 10-15% of malignant haemopathies and 1% of all cancers [1]. It affects preferentially subjects over 40 years with a peak frequency between 67 and 70 years [2]. Its main consequences are due to medullary tumor expansion and the production of large amounts of immunoglobulins or their toxic properties. The diagnosis of multiple myeloma is based on the association of a medullary plasmocytosis greater than 10%, a significant serum and / or urinary monoclonal immunoglobulin and clinical signs

related to malignant plasma proliferation. Although it remains incurable, scientific progress has led to improved patient management by introducing new diagnostic criteria and a better understanding of the heterogeneity of the evolutionary profile through the identification of new prognostic factors and To the development of new treatments [1,5]. The objective of this study is to study the epidemiological, clinical and biological characteristics of multiple myeloma through a series of 92 cases of patients collected at the Marrakech CHU Mohammed VI.

## MATERIALS AND METHOD

### Patients and methods:

This is a retrospective descriptive study over a 3-year period of 92 patients followed for multiple myeloma (January 2013 to December 2015). The diagnosis was based on the following data: medullary plasmocytosis, normal and dystrophic plasmocytes, presence of a monoclonal component in serum or urine, bone lesions compatible with that of multiple myeloma.

Each file was collected by means of a standardized collection sheet. The findings were: age, sex, background, occupation, exposure to toxic, clinical data. Biologically, all the biological tests performed: blood count (NFS), sedimentation rate (SV), serum protein electrophoresis (PPE), immunofixation, Bence Jones proteinuria research (BJ ), Myelogram and osteo-medullary biopsy as required, serum calcium, and creatinine.

## RESULT AND DISCUSSION

### Epidemiological data

We collected 92 patients with multiple myeloma. The sex ratio (m / f) was 1.3. The mean age of patients was 59.5 ± 12.5 years, with extremes ranging from 26 to 85 years. The distribution of patients by age is shown in Figure 1.

Farmers accounted for 13%, 10 were smoking, and 2 were alcoholics. 12 patients were diabetic, 8 hypertensive, 6 had kidney failure and 2 had TB treated. Clinically, bone manifestations were highest in 85.9% of cases (Table I).

### Hematological data:

Anemia was present in 64% of patients with hemoglobin less than 10 g / dl. It was normococcic normocytic regenerative in 96.7%, severe (Hb <8.5 g / dl) in 34.7%. Thrombocytopenia was present in 22.8%, while SV was accelerated in 70.6% of cases. A sternal puncture was performed in all patients. BOM was performed in 7 patients whose sternal puncture returned white or inconclusive. Significant medullary plasmocytosis ≥ 10% was found in 85% of the cases (n = 84); This plasmocytosis was made of dystrophic plasmocytes, plasmoblasts, proplasmocytes and lymphoplasmocytes (FIGS. 2, 3, 4). BOM confirmed the diagnosis in 6 cases, and was inconclusive in one case (Table I). The presence of a plasmacytoma was reported in 6 patients and was diagnosed by biopsies of bone tumors or by biopsy in case of spinal decompression.

### Immunochemical data

An EPP, immunofixation, and the search for Bence-Jones proteinuria were the rule in all patients. Ig was weighed in only 32 patients. The results of the electrophoresis of the blood proteins are illustrated in Table I.

Protein immunoelectrophoresis (IEPP) showed that IgG-type MM was the most frequent, in 67.9% (55 patients). The IgA-type MM was present in 23.8% of cases, while the light-chain myeloma was

found in 11%.

The search for BJ protein was performed in 32 patients, was absent in 3 patients and revealed a monoclonal ch chain in 11 patients, and a λ chain in 18 patients.

**Metabolic assessment:**

Hypercalcemia (> 150 mg / l) was observed in 22.8% (n = 21). Creatine levels were greater than 12 mg / l in 34.7% (n = 32).

**Prognostic scores**

The prognostic classification of Durie and Salmon showed that 65% of patients were class III, 22% class II and 13% class I.

**Discussion**

Although the MM has experienced significant progress in recent years in the management of patients, there is still an incurable haemopathy with a median survival rate of four to five years which tends to increase in recent years [6 , 7]. In this study, we studied the clinical, paraclinical and prognostic features of 92 cases of MM, collected at the Mohammed VI University Hospital in Marrakech.

The average age of our population is 59.9 years, 32.7% of whom are between the ages of 60 and 69, which is in perfect agreement with the literature [8-9]. The male predominance reported in the different series of literature (sex ratio H / F close to 1.4) [10] is verified in our series (sex ratio = 1.3).

To date, the causes of the GM are not yet fully elucidated. The only clearly identified risk factor is exposure to ionizing radiation [11]. Pesticides used in agricultural professions were also blamed. In our study, exposure to chemicals such as pesticides and tobacco are the main risk factors identified.

Plasmocytic infiltration is accompanied by osteoclastic resorption and inhibition of bone reconstructive function of osteoblasts. Bone symptoms were present in 85.9% of patients at diagnosis or later in the history of the disease, with a pathological fracture in 7.6%, complicated spinal cord compression in 7.6%, and Plasmacytoma in 6.5%, which corresponds to the data of the literature [6, 16].

Thrombocytopenia was present in 22.8%, whereas the rate of sedimentation (SV) was often high (70.6%), it was greater than 100 mm in 77.7% in the Tunisian series and in other studies [14, 16]. This phenomenon is directly related to the presence of the monoclonal protein. Anemic syndrome is one of the most frequent reasons for consulting multiple myeloma. It is present in 64% of patients, severe (Hb <8.5 g / dl) in 34.7%. Anemia is mainly due to medullary insufficiency associated with malignant plasma infiltration of bone marrow, haemodilution due to hyperproteinemia, and decreased secretion of erythropoietin (EPO) resulting from renal insufficiency [ 12].

The myelogram constitutes a decisive step in the diagnostic procedure of the MM, it makes it possible to demonstrate an abnormal plasmocyte infiltration quantitatively and qualitatively. The International MyelomaWorking Group IMWG 2014 distinguishes symptomatic MM (plasmocytosemédullaire more than 10%, often dystrophic, presence in a urine or urine of a monoclonal protein and the presence of an organic attack that can be attributed to Plasmacytic proliferation), Asymptomatic multiple myeloma and monoclonal gammopathies of undetermined significance (MGUS) [1].

The presence of morphological abnormalities, dystrophic plasmocytes or immature forms is also an important element for diagnosis. In our study, medullary infiltration was found in 85%, and was greater than 30% in 43.5% of the cases, mainly from dystrophic plasma cells. The BOM confirmed the diagnosis in 6 cases, and was inconclusive in one case. These results were close to those of the other studies (Table II).

The EPP showed a monoclonal peak in 88% of the cases. Our results are close to those of the study Boutay et al [6] where a monoclonal peak was detected in 76% of the patients. We observed a predominance of the IgG type (64% of the cases), followed by IgA (25% of cases) and light chains in 11%. No cases of MM to IgDni to IgM were detected. In our series, the distribution of isotypes of immunoglobulins and light chains is close to that reported by other series [13, 6].

Creatinemia and serum calcium are essential to assess the possible complications of multiple myeloma. Hypercalcemia and elevation of serum creatinine were present in 22.8% and 34.7%, respectively. Results close to those of other series [6, 14].

The Salmon and Durie classification was the benchmark for prognosis assessment. It makes it possible to evaluate the tumor mass as a function of the level of the monoclonal components and the rating of the bone lesions.

According to this classification, 57% of our patients are classified stage III, 22% stage II and 13% stage I. This rate varied markedly between the different studies. In the study of NDOMOCRAH A et al [15], the cases of MM stage III showed 66.7%, while it is of the order of 100% in the Tunisian study. In our study, the rate remains high but lower than in the other series, this can be explained by the young age of the patients and the diagnosis that is made at early stages of the disease. This predominance of stage III has been noted in other series.

In our work, the medullary karyotype was not performed in any patient; This is due to the lack of resources in our patients.

## CONCLUSION

MM is a condition characterized by its clinical and biological polymorphism. It is easy to diagnose, but it still poses therapeutic difficulties. The prescription of an EPP supplemented by immunofixation before an acceleration of SV, anemia or hypercalcaemia will allow an early diagnosis and a better prognosis. The myelogram, essential for diagnosis, remains a decisive step on the one hand to confirm the Plasmacytic infiltration and on the other hand to assess the importance of infiltration and the presence of dystrophic forms. It was noted a high percentage of advanced stages but remains less than that in the other series, This is correlated with delayed consultation and diagnosis for the majority of our patients. This study needs to be continued in order to better determine clinical and paraclinical characteristics by age group and to better identify the factors of poor prognosis by the systematic realization of a systematic medullary karyotype.

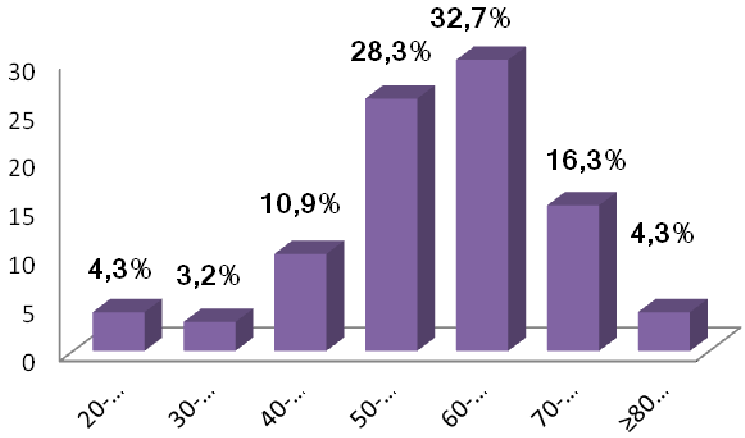
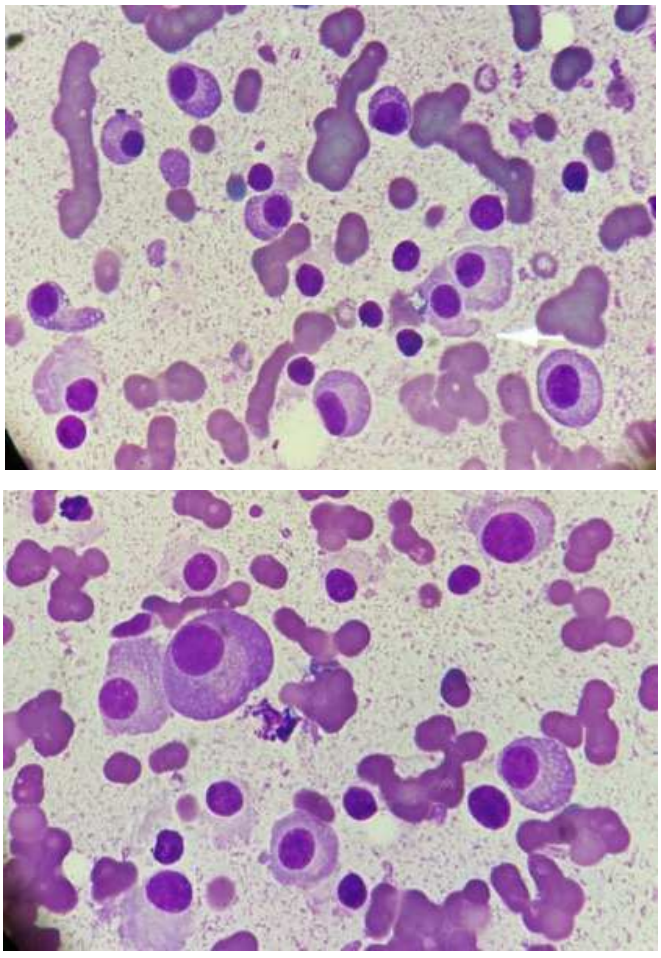



**Figure** 1: Patient distribution by age (n = 92)

**FIGS. 2, 3 and 4:** different cytological aspects of bone marrow plasmacytosis



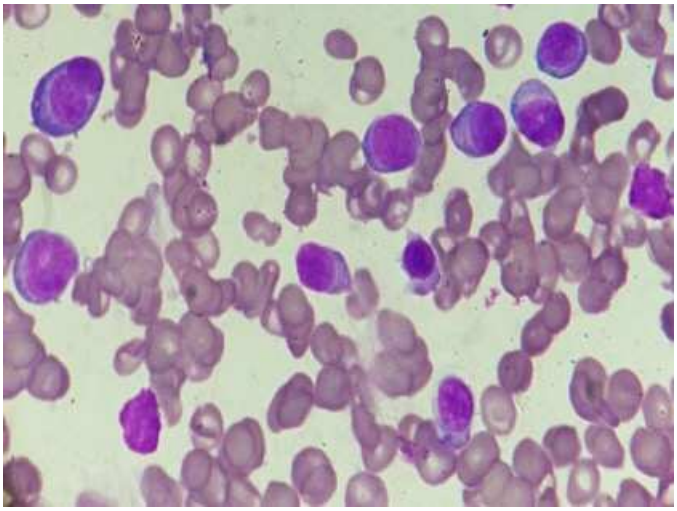


**Table I:** Circumstances of discovery and biological parameters of multiple myeloma in the study population (n = 92):

| | | Settings | Numberof Patients | *Frequency (%)* |
|---|---|---|---|---|
| Diagnostic Circumstances | | Bone pain | 79 | 85,9 |
| | | Pathological Fracture | 7 | 7,6 |
| | | Bone swelling | 5 | 5,5 |
| | | Anemic syndrome | 39 | 42,4 |
| | | General Condition Alteration | 43 | 46,8 |
| | | Spinal cord compression | 7 | 7,6 |
| | | plasmacytoma | 6 | 6,5 |
| Biology report | Hemoglobin <12g / dl | Hémoglobine <12g/dl | 59 | 64 |
| | Plates <120 / mm3 | Plaquettes < 120/mm3 | 21 | 22,8 |
| | Plasma cell infiltration> 30% | Infiltration plasmocytaire >30% | 40 | 43,5 |
| | Plasmocytic infiltration 10-30% | Infiltration plasmocytaire 10-30% | 44 | 47,8 |
| | Plasma cell infiltration <10% | Infiltration plasmocytaire <10% | 8 | 8,7 |
| | BOM | BOM | 7 | 7,6 |
| | > 100mm | >100mm | 65 | 70,6 |
| | Protein> 80g / l | Protidémie > 80g/l | 72 | 78,2 |
| | Monoclonal peak: Gamma area | Pic monoclonal : Zone gamma | 55 | 67,9 |
| | Monoclonal Peak: Zone beta | Pic monoclonal : Zone beta | 20 | 24,7 |
| | Monoclonal peak: Alpha zone | Pic monoclonal : Zone alpha | 6 | 7,4 |
| | hypogammaglobulinemia | hypogammaglobulinémie | 5 | 5,4 |
| | | EPP normal | 6 | 6,5 |

**Table II**: Comparative study of the results of our study with that of other studies

| | H. HAMDANI et al 2016 (Marrakech) | Amrani Hassani M et all 2010 (casablanca) [13]. | Boutay A et all 2012 (tunis) [6]. | KAKPOVI K et al 2014 (togo) [14]. | N DOMOCRAH A et al 2013( Bangui) [15]KakpoviKodjo, |
|---|---|---|---|---|---|
| **Number of patients** | 92 | 10 | 54 | 2881 | 15 |
| **Duration of study (years)** | 3 | 1 | 3 | 21 | 6 |
| **Average age (years)** | 59,5 | 59 | 67 | 56 | 66,8 |
| **Sex ratio** | 1,3 | 1,3 | 1,7 | 1,1 | 6,5 |
| **Number of growers (%)** | 13 | - | 9,2 | - | 59,8 |
| ***The clinic (%)*** | | | | | |
| *-Bone pain* | 85,9 | 80 | 74,1 | 93,2 | 79,9 |
| *-Syndrome Anemia* | 64 | 80 | 37 | - | 40 |
| *-Alteration of the general state* | 46,8 | 30 | 31,5 | 76,3 | 46,7 |
| *- medullary compression* | 7,6 | - | 11,1 | 20,3 | 20 |
| *-plasmacytoma* | 6,5 | - | 9,3 | - | - |
| ***Hematological data (%)*** | | | | | |
| *-anemia* | 64 | 80 | 87 | - | 53,8 |
| *-thrombopénie* | 22,8 | - | 33,3 | - | 6,7 |
| *-vs accelerated* | 70,6 | 100 | 77,7 | - | 93,3 |
| *-Pilmocytic infiltration* | 85 | 100 | 76 | - | 100 |
| ***EPP:*** | | | | | |
| *-pic monoclonal* | 88 | - | 76 | - | - |
| *-type of the MM:* | | | | | |
| *Ig G* | 64 | 50 | 61,8 | - | - |
| *Ig A* | 25 | 30 | 29,4 | - | - |
| *Light Chains* | 11 | 20 | 5,9 | - | - |
| ***Metabolic assessment:*** | 22,8 | - | 26 | 28,8 | 60 |
| *Hypercalcemia> 150mg* | 34,7 | - | 19 | 32,2 | - |
| *Creatinine> 12mg* | | | | | |
| ***Prognostic score:*** *Stage III Salmon and Durie* | 57 | 80 | 100 | 86 | 66,7 |

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