Advances in Bioresearch
Adv. Biores., Vol 10 (2) March 2019: 40-49
©2019 Society of Education, India
Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.10.2.4049

Advances in Bioresearch

ORIGINAL ARTICLE

Retrospective Analysis of Multiple Myeloma Cases in Esatern Algeria

[1]Aziez Chettoum, [2]Kamilia Guedri , [3]Rachid Mosbah, [4,5]Zouhir Djerrou, [1]Chafia Labed
[1]Department of Biology Animal, Faculty of Nature and Life Science, University Mentouri Constantine, Algeria
[2]Department of Applied Biology, University Larbi Tebessi, Tebessa 12000, Algeria
[3]Department of Biology, University of Boumerdes, Boumerdes 35000, Algeria
[4]Department of Nature and Life Sciences, Faculty of Sciences, University of August 20th 1955, Skikda, Algeria
[5]Laboratory of Pharmacology and Toxicology, University of Mentouri Constantine 1, Algeria

ABSTRACT
Multiple myeloma or kahler's disease is a hemopathy characterized by monoclonal malignant plasmocytic proliferation. The aim of our work is to specify the clinical, paraclinical and prognostic characteristics of multiple myeloma in eastern Algeria through a retrospective study. This is a retrospective and analytical study, involving 53 multiple myeloma cases, spread over a period of 8 years, from the year 2010 to March 2018, carried out within the department of Hematology and Oncology of the Military Regional University Hospital of Constantine. The average age of our patients was 62 years and the sex ratio (W / M) of 1.41. Bone pain revealed the disease in 33.96% of patients, followed by anemic syndrome (30.19%). Osteolytic radiological lesions were present in 60.7% of patients. The diagnosis was made by the myelogram in 90.75% of the cases where it objectified a dystrophic medullary plasmocytosis in 66.66% of the cases. The medullary infiltration rate of plasma cells was 33 ± 23%, and serum protein electrophoresis showed the monoclonal peak in 86.79% of cases, with a predominance of IgGk isotype found in 67.57 % of cases. According to the classification of Salmon and Durie 85% of patients are classified in stage III. In this study, we found that the relationship between pesticide effect and disease is obvious, thanks to the high rate of sick in areas with high agricultural activity. This study is limited and the results obtained cannot be generalized to the general population. However, this should encourage us to work to improve the management of patients by introducing new techniques for early diagnosis and effective new treatment.
Keywords: *Multiple myeloma, plasmocytosis, immunotoxification, pesticides.*

Received 04.01.2019 Revised 18.01.2019 Accepted 06.02.2019

How to cite this article:
Chettoum A, Guedri K, Mosbah R, Djerrou Z, Labed C. Retrospective analysis of multiple myeloma cases in Eastern Algeria. Adv. Biores. Vol 10 [2] March 2019: 40-49

INTRODUCTION

Despite recent advances in the early diagnosis and management of cancer pathology, the cancer remains the first cause of death in Algeria after cardiovascular disease and high blood pressure. We noted a rate increase of hematological malignancies that currently accounts for 10% of cancer pathology.

Today we are interested in cancer of multiple myeloma; it represents 10% of hematological malignancies and 1% of all cancers. It is not a public health problem because of their low incidence, favorable prognosis and low mortality.

Multiple myeloma (MM), also known as Kahler's disease, is an incurably disease of the bone marrow. It is characterized by the uncontrolled growth of clonal plasma cells (PCs) and leads to production of non-functional gammaglobulin [1], it is actually the second most common blood cancer after non-Hodgkin's lymphoma [2].

The aim of our study is to carry out a retrospective investigation, in hematology and oncology service of the Constantine University Regional Military Hospital, in patients with multiple myeloma in different regions of eastern Algeria, with the aim to explore the implication of this pathology.

MATERIAL AND METHODS

Patients. A total of 53 MM patients who fulfilled Multiple Myeloma criteria performed within the department of hematology and oncology at the Constantine Military Hospital in Algeria were enrolled from January 2010 to March 2018. In accordance with the protocol approved by the Medical Ethics Committee at the Constantine Military Hospital, retrospective analyses were carried out on the patient's data.

All patients data included in our work would have at least two of the following criteria: Presence of a monoclonal immunoglobulin in serum or urine whatever its concentration, and the presence of a medullary plasmocytosis greater than 10%, presence of one of the elements CRAB (hypercalcemia, renal failure, anemia, bone involvement).

Other types of hematological malignancies were excluded from our study. Patients with Kahler's disease with incomplete or unusable data are systematically excluded.

Several parameters were collected for each patient (age, gendre, origin, presence or absence of antecedents, clinical and biological data).

Statistical analysis was performed using statistical software SPSS 20 was used for statistical analysis. All values are presented as mean ± S.E.M.

RESULTS

Clinical features

Age and sex distribution: Of the 53 patients with MM, (41.51%) were male and (58.49) were female (Fig. 1). The median patient age was 62 years (range, 60-69).

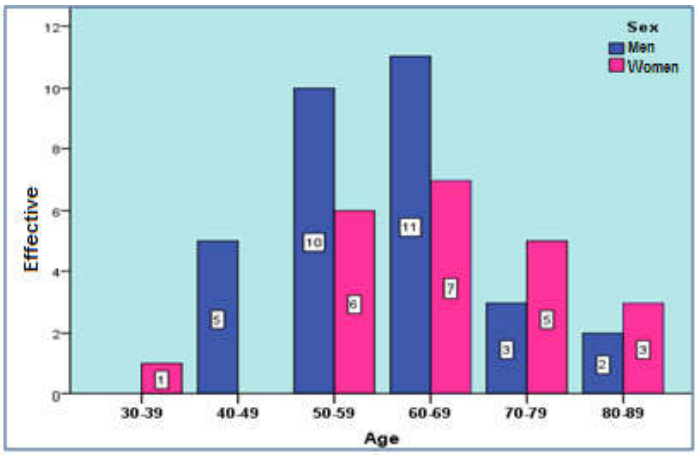

Figure 1: Age and sex distribution of MM

Residence distribution: In our study, most patients come from the Eastern Algerian are residing in the wilaya of Jijel with 11 patients or 24.4% of cases, followed by Mila and Guelma with 5 patients or 11.1% of cases (Fig. 2).

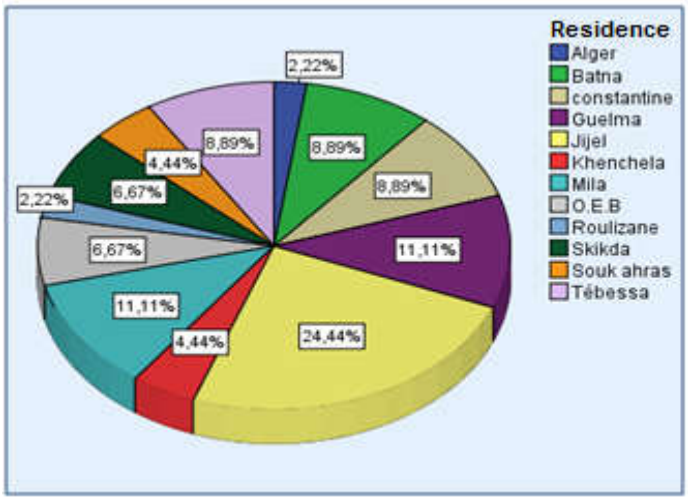

Figure 2: Distribution of patients by country of residence

Antecedents: It was not that 56.6% of patients had medical ACDS associated with surgical procedures, and the most common diseases were hypertension in 7 patients (13.21% of cases), followed by diabetes in 5 patients (9.4%), and 10 patients (18.9%) achieved by other pathology different. For family history it was noted that in 1 only there was a concept of pulmonary disease (Fig. 3).

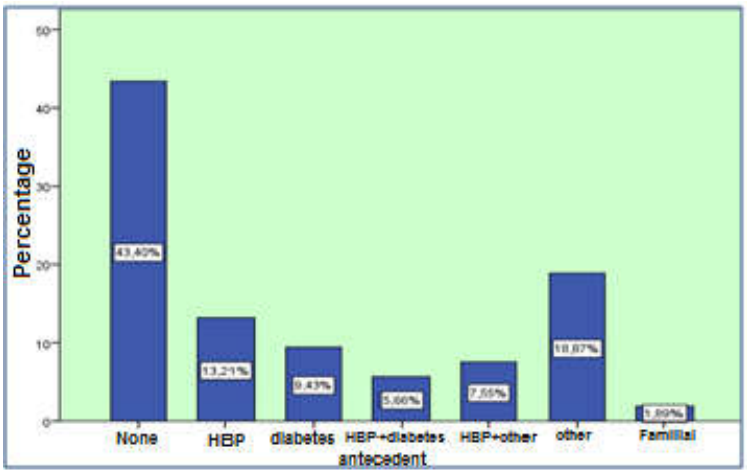

Fig 3. Distribution of patients by personal and family history

Distribution of MM cases according to toxic habit: We can see from the above section that the majority of the cases in our 53 patient's series have no toxic habit; of the 5 remains we have 4 smokers and 1 smoker and alcoholic, 7% and 2% respectively (Fig. 4).

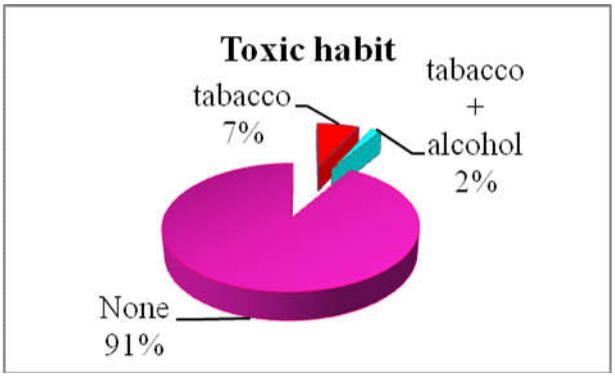

Fig 4 : Distribution of MM cases by toxic habit

Distribution of MM cases by reason of consultation: From the above histogram we can be concluded that the bone attacks represents the highest tell-tale sign of the disease with a percentage of 33.96%, the anemic SD come second with a percentage of 30.19%, the SD infectious revealed the disease in 5.66% of cases, 3.77% of patients revealed their disease by a hemorrhagic SD, 26.42% of cases with no telltale sign (Fig. 5).

Radiological examination: All patients benefited from a radiological assessment involving X-ray radiography and computed tomography (CT), magnetic resonance imaging (MRI). The result of radiological examination specified in 53 patients among whom 60.7% of the patients had bone lesions, 17.9% of the patients had fractures and 21.4% patients had vertebral compression.

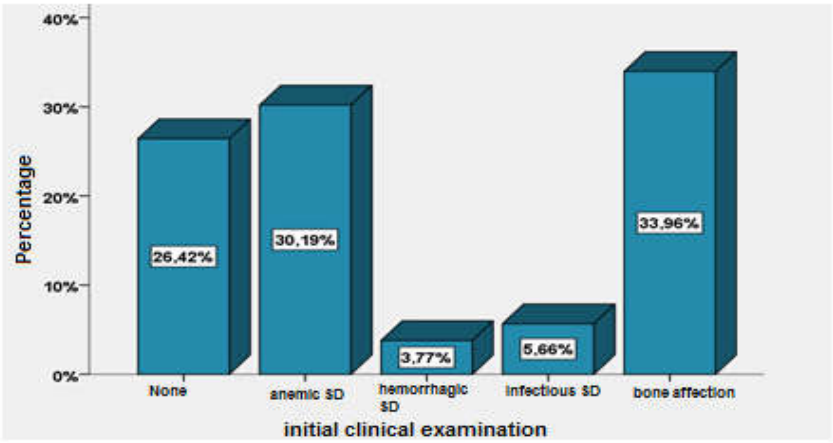

Figure 5: patient distribution according to clinical demonstration

Hematological data:
Sedimentation rate (ESR)
The ESR was accelerated in the first hour in all patients, in 43.59% of cases is greater than 100mm / h, the average rate of ESR in our series is 87.62 ± 44.2 mm / h1 with extremes from 6 to 153mm/h (Fig. 6).

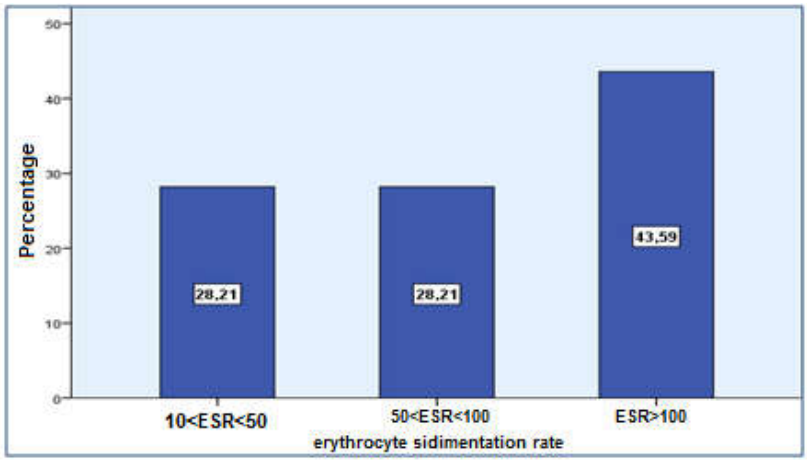

Fig 6. Distribution of MM cases according to ESR

Hemoglobin: In our series, 20.76% of patients had anemia with an Hb level ≤7, the average rate of Hb was 9.89g / dl ± 2.63 g / dl with extremes of 5.8 to 15.9 g / dl (Table 1).

Table 1. Variation of hemoglobin

Hemoglobin level (g/dl)	Effectives	Percentage(%)
5g/dl < Hb < 7 g/dl	11	20,76%
7g/dl < Hb < 12 g/dl	33	62,26%
Hb > 12g/dl	9	16,98%
Total	53	100%

White blood cells (WBCs): It was noted that 18.86% of patients had leukopenia (n = 10) with WBC <4g / l and 26.41% of patients had leukocytosis (n = 14) with WBC > 10g / l, the average leukocyte count was 7459 el / mm^3 ± 3123 with extremes of 2200 to 14000 el / mm^3 (Table 2).

Table 2. Variation of white blood cells

WBCs (g/l)	Effectives	Percentage (%)
WBC <4 g/l	10	18,86%
4g/l < WBC < 10g/l	30	56,6%
WBC > 10g/l	14	26,41%
Total	53	100%

Platelet count: The platelet count was normal in 37 patients or 69.81% of cases and thrombocytopenia was found in 12 patients, or 22.64% of cases, thrombocytosis in 4 patients, or 7.54% of cases (Table 3).

Table 3. Variation of platelet count

Platelet level (g/l)	Effectives	Percentage (%)
PQ < 150g/l	12	22,64%
150g/l < PQ < 400g/l	37	69,81%
PQ > 400g/l	4	7,54%
Total	53	100%

Fig 7: Myelogram distribution.

Myelogram: The myelogram was performed in 53 cases, of which 47 cases (88.67%) have cell richness of abnormal medullary plasma; most are dystrophic with plasma infiltration ≥ 10% (Figure 7).

Immunochemical data:

Serum protein electrophoresis (EPPS): The monoclonal peak was found in 46 patients, 86.79% of the cases with migration to the gamma globulin zone (ɣ) in 69.57% of cases, and migration to the bita zone (β) in 21.74% cases, and hypogamaglobulinemia was observed in 4 patients, 8.7% of patients (Figure 8).

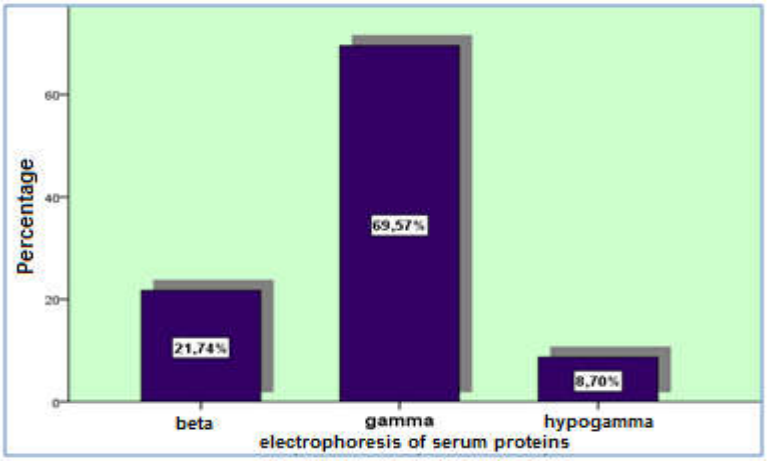

Fig 8. Patient distribution according to the monoclonal peak

Serum Protein Immunofixation: Immunofixation was performed in 53 patients, with IgG frequent in 79, 07% of cases, followed by IgA in 18, 60% of cases and IgD in 2.33% of cases (Figure 9).

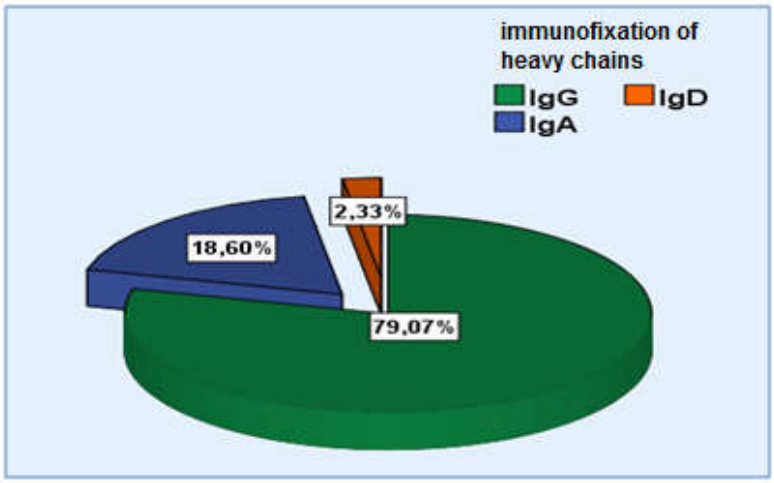

Fig 9. Patient distribution according to immunofixation results of serum proteins.

Distribution by type of light chain: Depending on the type of light chain one can conclude according to the histogram that: Kappa light chains are majority and more frequent (71, 43%) than lambda (28, 53%) (Figure 10).

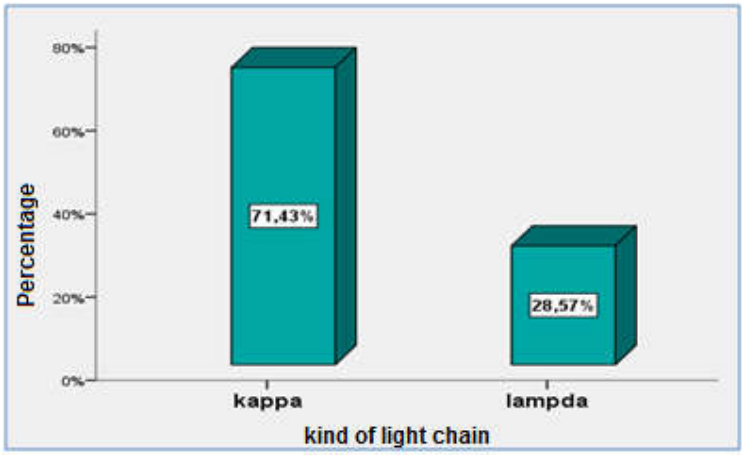

Fig 10. Distribution of cases by type of light chain.

Renal function: The renal record was performed in 53 patients, showing that 45.45% of cases had renal failure (Figure 11).

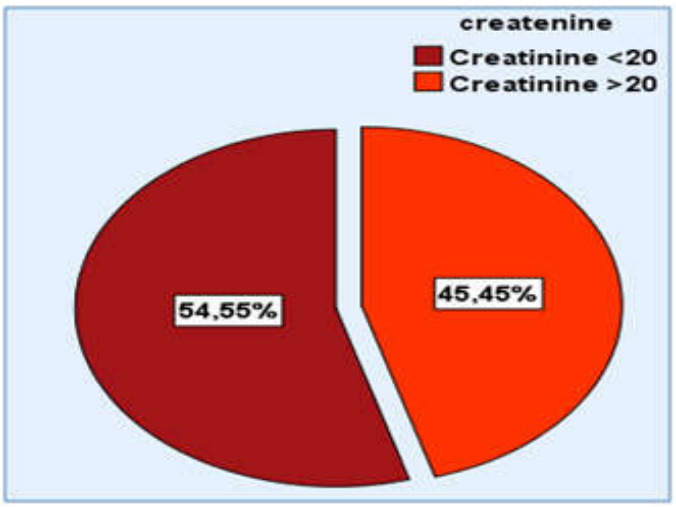

Fig 11. Distribution of patients by renal function

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Prognostic Classification:

Durie Salmon Classification: Before finding that the majority of patients consult at an advanced stage (Stage III) with a percentage of 85% of which 56% are at IIIA stage and 29% are at IIIB stage. Patients in stages I and II are very rarely found to be 6% and 9% respectively (Figure 12).

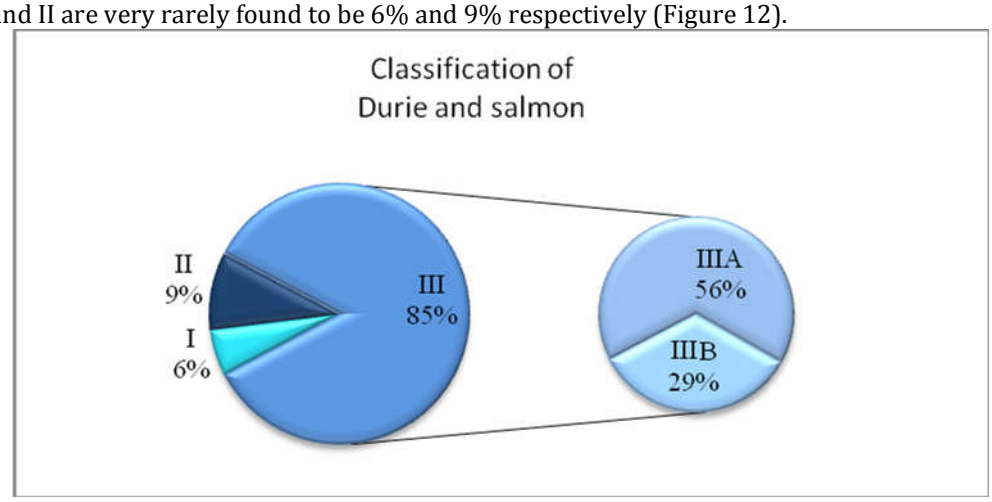

Fig 12. Patient distribution according to Durie Salmon classification.

Evolution: The evolution of patients after chemotherapy was not specified in 21 patients (39.62%) with partial remission in 14 patients (66.7%) (Figure 13).

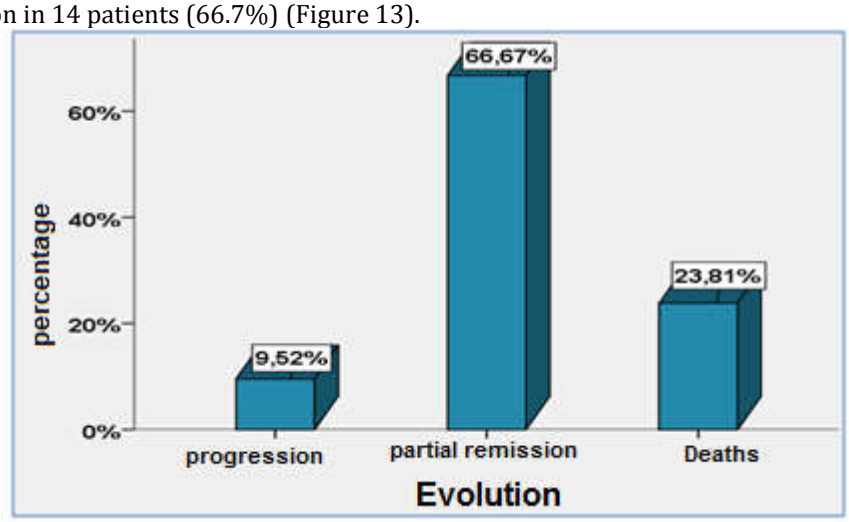

Fig13. Distribution of patients by outcome after treatment

DISCUSSION

This was a retrospective study, which consisted of analyzing the data of cases diagnosed and treated by MM during the period 2010 to February 2018 to the clinical hematology service of Constantine HMRU. These data were obtained after counting medical's data and cytological review reports.

Reported data may not reflect the situation in the general population. Indeed, the actual strength of MM during our study period could be underestimated. Despite these limitations, the study assessed the main epidemiological, clinical and cytological characteristics of MM during this period in the eastern region of Algeria.

Age distribution was treated by several authors; in our work the age range was significant between 60 and 69 years old with an average age of 62.43 years and a median of 62 years at the time of diagnosis for the 2 sexes.

Our results are comparable to the study in a Moroccan population published by D. Jeddi *et al* in 2011 that the average myeloma age of 62.7 years [4], and rapproched to the study of Koffi *et al* in 2000 in Africa which also found the average age of patients was 58 years [5]. In Tunisia the average age of ptients was 67 years according to the study by Bouatay *et al* in 2012.

In the study of Zouaoui et al. in the Western Algeria during the period 2002-2012, the median age of patients was 60 years for both sexes [7]

Our result is similar with a study of Togolese population that was published by Kokpovi and al. (2014). [8]. But the research plow shows that the risk of this disease is increasing with age. In our study no

children affected by the MM. These data are correlated with literature because Koffi *et al* in 2000 publish in Africa the same results [9].

In our study, we noted a slight female dominance with a rate of 58.49% compared with 41.51% of male cases, with a sex ratio (F/H) 1.4, these results in accordance with Béatrice Chombart *et al* in 2005, which in France also found the sex ratio 1,48 [10]. And do not deal with several publications, Tunisian studies made by Slaheddine Chkir *et al* in 2010 which regained male dominance with the sex ratio (H/F) of 1.1 [11]

This could be explained by the predominant sex in the general population of the study area. The distribution of patients by origin was revealed that wilaya of Jijel by 24.4% of patients, Mila and Guelma by 11.1% of patients.

Jijel, Guelma, and Mila are classified among the country, as the agricultural population is frequently more exposed to pesticides, so this could explain the increased risk of disease in the agricultural regions. This finding is supported by the Epidemiological Literature on the Risks of Multiple Myeloma in Connection with Occupational Exposure to Pesticides has been systematically reviewed by several authors who conducted meta-analyzes. Between 1992 and 2009, six meta-analyzes were published [12, 13, 14, 15, 16, 17]. Of these, two relate specifically to multiple myeloma [13, 16], one on hematopoietic cancers [15] and three cover all cancers but also show results for each type of cancer individually [12, 14, 17]. The number of epidemiological investigations included in these meta-analyzes ranged from 2 to 32 and was published between 1970 and 2007.

By referring to the types of professional activities considered, four meta-analyzes relate to exposure in the agricultural sector [12, 13, 14, 16], Overall, all show a risk increase of multiple myeloma from 9% to 39% among professionals exposed to pesticides compared to the general population .

In our series, 56.6% of patients present medical histories associated with different surgical procedures (chalecystectomy, prostate, appendictomy…), among which 20 patients had HTA associated with type 1 or 2 diabetes with type 1 or 2 diabetes, with other pathologies for this. achieved by the MM We observed that 1.9% of our sample had a family history that had a concept of lung disease. .

Our results are correlated with literature, Yasar Albushra Abdul Rahiem Ahmed *et al* were published in 2013 the relationship between diabetes and multiple myeloma [18], and Jukka Lehtonen *et al* in 2007 were confirmed the relationship of pulmonary hypertension with multiple myeloma in a patient of 48 years [19]. And many investigators confirmed the relationship of these pathology with the multiple myeloma[20, 21, 22].

In our series, the most common manifestations of MM are bone events 33.96% of cases, the anemic 30.19% syndrome, hemorrhagic syndrome in 3.77% of cases and infectious syndrome 5.66% of cases.

These results deal with the literature that bone manifestations are the most common mode of revelation of the MM. Bone demonstrations are very frequent. They are clinically detectable in 69% of the general population according to the study of Brahem et al, 2015 in Tunisia [1].

In our work, all patients make a radiological examination, we observed that the dominant bone lesions in the radiological examination table by 60.7% of patients followed by vertebral settlement in 21.4% of patients and fractures in 17.9% of patients. These results converge with A. Bouatay *et al* (2012) which show the same classification of radiological signs which also find bone lesion in 50%, followed by vertebral settlement in 13% and fracture in 7.4% [23].

The complications of the most observed MM in our series are bone dolphins in 40.9% of patients and renal failure in 31.8% of patients, followed by hypercalcemia in 13.6% of patients.

This results are according with the work of Gay *et al* (2010) showed that 66% of bone sinkers, 30% renal failure and 13% hypercalcemia [24].

In our series, the results of the ESR have been specified in all patients, the average rate in first hour is 87.62 ± 44.2 mm at an extreme of 6 to 153 mm The accelerated sedimentation rate is the most reported form in literature as the study by Braheme *et al* (2015) which shows the average rate of the VS was 100 mm [27]. Further study by Chkir *et al* (2010) and Gaougaou *et al* (2014) which also finds the acceleration of the ESR from 73 to 85% of cases [11, 25].

In our study, the average hemoglobin rate estimated at 9.89 ± 2.63 g/dl has an extreme of 5.8 to 15.9 g/dl. 17.6% of patients had Hb ≤ 7, due to anemia. These results agreement with the study by A. Laanani *et al* (2013) which prove almost the same result [26]. Tendis that the average rate of white cells 7459 ± 3123 element/mm ^{3} is extreme from 2200 to 14000 el/mm^3. 19.6% of patients had a rate of ≤ 4 g/l that was explained by leucopenia, and 23.5% of patients showed Thrombopenia these results was according with literature [11, 25].

In our results 66.66% of cases showed dystrophic medullate plasmocytosis, the average rate of total medullary infiltration 33 ± 23% has an extreme of 1% to 100%. These data agreement with literature

which also finds the same results [11, 27, 25]. In our series, the monoclonal peak was found in 86.79% of patients and observed that the predominance of migration to the gamma zone by 67.39% of cases and a minority of hypogammaglobulin in 8.7% of cases. These results agreement with Ngolet Lo *et al* (2016) which publish the same values of EPPS [28]. The same result was found by many investigators [26, 29].

The immunofixation of serum proteins was specified in 81.13% of cases and the distribution of our patients shows that the most dominant igg isotype by a frequency of 79.1% of the cases, by contrast 2.3% of patients have a IgD peak, and does not find any IgM peak that explains that IgM and IgD peak were rare. We observed that 71.43% of patients have a light kappa chain. These results were in agreement with many literature studies [33, 29, 8, 7]

In our series, the average creatinine rate estimated at 27 ± 30.6 mg/dl has an extreme of 5.6 to 118 mg/dl. Observed that 45.45% of patients have an abnormal creatinine level 20 mg/dl explaining the number of patients affected by renal failure

These results are very high compared with the results of Zouaoui *et al* (2013) which shows that Créat > 20mg/dl in 28% of patients. [7]

In our series, the classification of the MM is based on the classification of Durie Salmon. The distribution of our patients according to stage shows that 69.8% of the patients classified in Stage III of which 50.9% of patients at stage IIIA and 18.9% of patients at stage IIIB stage IIIB, while 15.1% of patients at stage I and 9.4% of patients at IIA stage, 5.7% of patients MGUS early stage of MM. These results were assimilated with other studies in literature [9,27]. These independent results with renal function results as the latter not specified in all patients. We observed that 66.7% of our sample has partial remission could be explained by an improvement in treatment.

In this study, we found that the relationship between pesticide effect and disease is obvious, thanks to the high rate of sick in areas with high agricultural activity.

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