The type of manuscript : original article

Interest of serum and urine assays in the diagnosis and control of multiple myeloma

Abstract

Introduction : Multiple myeloma or Kahler's disease is a haematological disorder characterised by the proliferation of an abnormal plasma cell clone secreting monoclonal immunoglobulin in the marrow.

Patients and methods : This is a descreptive and analytical study carried out in the West Algerian region over a 3-year.

Results and discussion : The epidemiological study revealed that hypoalbuminemia, hyperprotidemia and hypercalcaemia are common in the majority of patients. We also noted a predominant migration of immunoglobulins in the gamma zone. On the other, On the haematological level we recorded anaemia, leukopenia, the presence of red blood cells in rolls and malignant plasma cells.

Conclusion : This study provided biological and epidemiological data on multiple myeloma. The clinical and biological profile of the myeloma patients in our study is similar to that found by most research teams.

Key words : Multiple myeloma, hypo-albuminemia, leukopenia, malignant plasma cells.

Inroduction

Multiple myeloma or Kahler's disease is a haematological malignancy characterised by the proliferation of an abnormal plasma cell clone secreting monoclonal immunoglobulin in the bone marrow **(1).** Multiple myeloma accounts for 80% of malignant monoclonal gammopathies and about 10% of haematological cancers and about 2% of all cancer deaths **(2).** Multiple myeloma (MM) affects slightly more men (45%) than women (46%), and the median age at diagnosis is about 70 years. On the other, it can affect young subjects with a percentage of 2.8% **(3).**

The annual incidence in Algeria is 0.9 to 1.1/100 000 inhabitants per year **(4).** The etiology of multiple myeloma is still unknown, several publications have been devoted to risk factors, often with uncertain and controversial conclusions **(3).** The only clearly identified risk factor is exposure to ionising radiation **(5).**

The diagnostic criteria were updated by the International Myeloma Working Group in 2013. However, the criteria are based on monoclonal plasma cell infiltration followed by

identification of the type of myeloma if it is symptomatic or asymptomatic, determination of infections and hyperviscosity syndrome **(7).**

The majority of patients with multiple myeloma go through a transient pre-myeloma state, the main types of which are indeterminate monoclonal gammopathy (MGUS) and asymptomatic multiple myeloma **(1).**

Biology plays an important role in the diagnosis and management of myeloma patients. Biological examinations allow the classification of patients into different groups from which the management and therapeutic follow-up is derived. The initial work-up of myeloma patients includes a complete blood count, a peri-herbal blood smear, a full chemistry work-up including electrolytes, albumin and liver and kidney function **(6).**

On the other, the diagnosis of multiple myeloma is based on a precise definition: the presence of a serum or urine monoclonal immunoglobulin, a bone marrow plasmacytosis with a rate ≥ 10% and/or the presence of organic lesions directly attributable to dystrophic plasma cells **(8).** However, serum and urine protein electrophoresis, serum immunfixation and serum free light chain assay are very important for the diagnosis of multiple myeloma **(6).**

The aim of our study is to determine the epidemiological, clinical and biological aspects as well as to evaluate the biochemical profile of patients with multiple myeloma in the Western Algerian region.

Patients and methods

This is a descriptive and analytical study carried out in the West Algerian region over a period of 3 years. The study population is composed of 100 subjects suffering from multiple myeloma. This study was carried out in collaboration with the anti-cancer centre of sidi bel abbes

Patients included: An exploitation form was made for each patient during the analysis of his medical file. It allows us to identify :

- Epidemiological characteristics: age, sex, origin
- Clinical information : reasons for hospitalisation, pathological history.

The parameters analysed in this study are mainly :

Protein assessment, in particular protidemia, serum protein electrophoresis (SPE), serum immunotyping, Immunoglobulin (Ig) weight measurement, identification of Bence Jones Proteinuria (BJP) and 24-hour proteinuria, creatinine.

Haematological assessment : sedimentation rate (ESR), complete blood count (CBC), myelogram, β 2 microglobulin, C-reactive protein (CRP) and lactic dehydrogenase (LDH).

All data were recorded and analysed using IBM SPSS version 25

Results and discussion

1. Age distribution

The average of our patients at the time of diagnosis was 61.66 years with extremes from 40 to 70 years. The highest frequency was recorded in the age group between 61 and 70 years with 40% of cases.

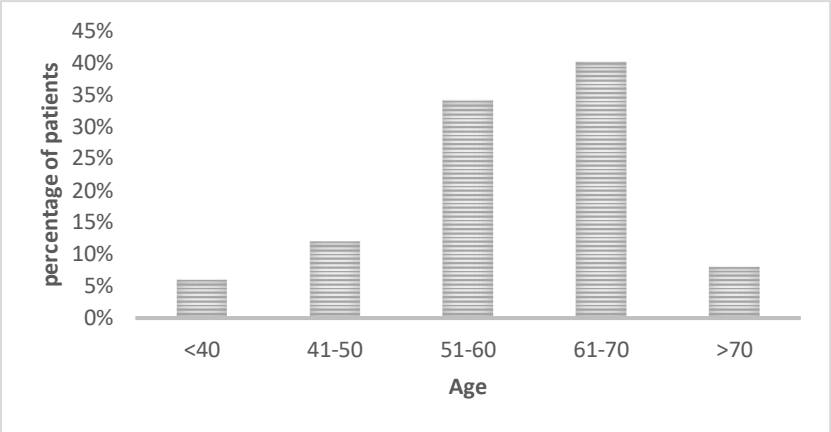

Figure N°01 : Histogram representing the distribution of patients by age

2. Distribution by gender

Our series includes 53 men and 47 women, respectively 53% and 47% of all cases with a sex ratio (M/F) of 1.13 in favour of men.

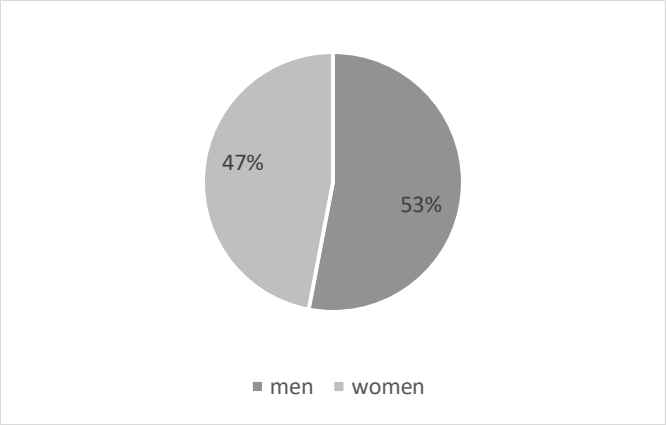

Figure N° 02 : Distribution of patients by gender

3. Circumstances of discovery

The clinical manifestations of multiple myeloma are numerous, Most often it is a bone disorder, the alteration of the patient's general condition. Rarely patients come into a stage of complications as infections or renal failure.

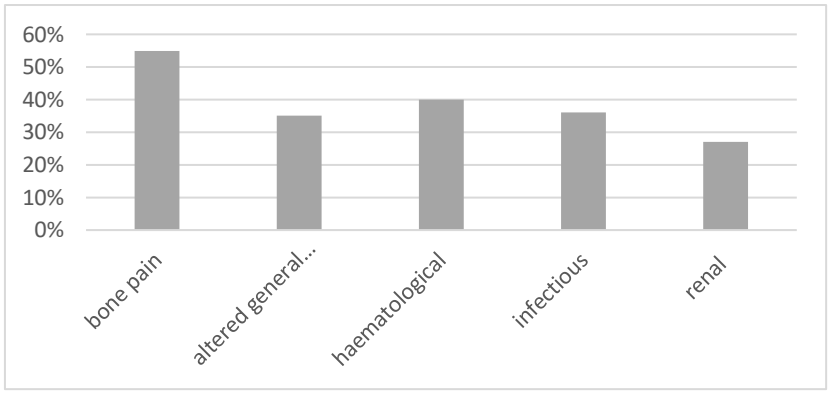

Figure N°03: Distribution of patients according to the main clinical manifestations.

4. Protidemia

The next figure represents the distribution of patients according to the total protein level, in our series hyper-protidemia was found in 55% of the cases.

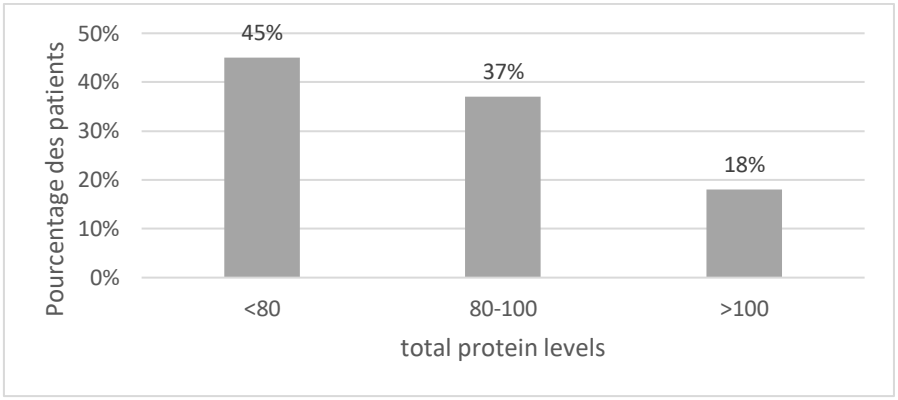

Figure N°04 : Distribution of patients according to protidemia (g/dl).

5. Serum protein electrophoresis

In this study we have registered a predominance of paraproteins migrating in gamma globulin zone with 70% followed by paraproteins migrating in beta globulin with 45% and with 39% of paraproteins migrating in alpha2-globulin.

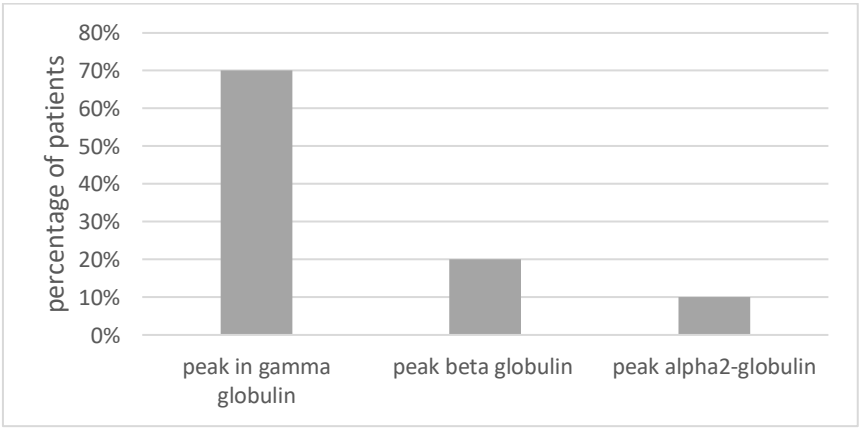

Figure N° 05 : Distribution of patients according to the migration of the monoclonal peak in serum protein electrophoresis.

6. Immunofixation of serum and urine proteins

Data analysis reveals that 61% of patients are type IgG, 30% are type IgA and 9% are type Light Chain (LC).

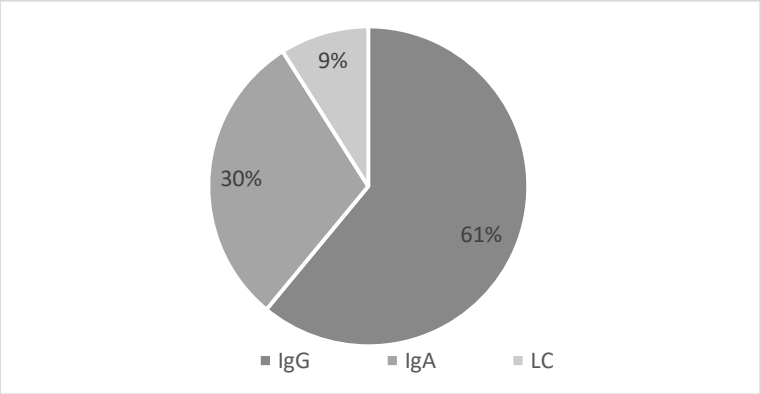

Figure N° 06 : Distribution of patients by multiple myeloma isotype.

The next table represents the distribution of patients according to the type of light chain. In this series we recorded a predominance of the kappa light chain with 66% compared to 34% for the lambda light chain with a κ/λ ratio of 1.94.

Table 1 : Distribution of patients by light chain type.

Type of light chain	Kappa type			Lambda type			Kappa/Lambda ratio
	IgG	IgA	LC	IgG	IgA	LC	
Number of cases	40	22	4	21	8	5	1.94
Total	66			34			
Percentage(%)	66%			34%			1.94%

7. Calcemia

In our present study, hypercalcaemia was recorded in 66% of patients, including 21% with major hypercalcaemia (>120mg/l).

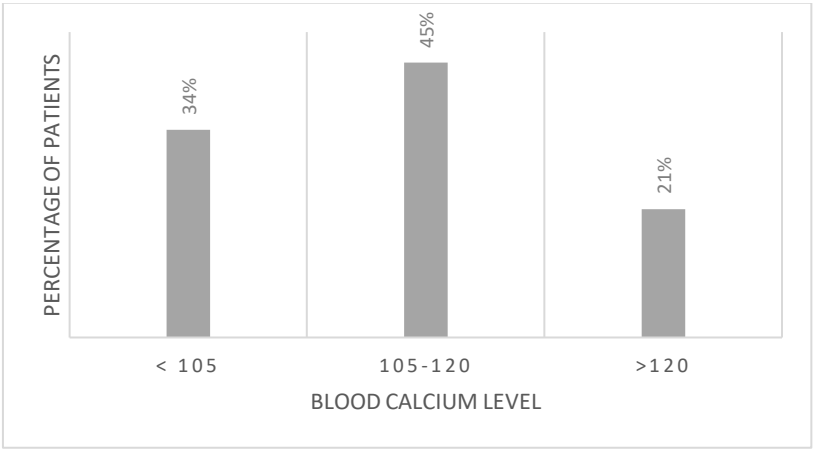

Figure N°07 : Distribution of patients according to the level of Calcemia (mg/l).

8. Albuminemia

The next figure represents the distribution of patients according to albumin levels. In this series, 74% of the patients were found to be hypo-albuminemic.

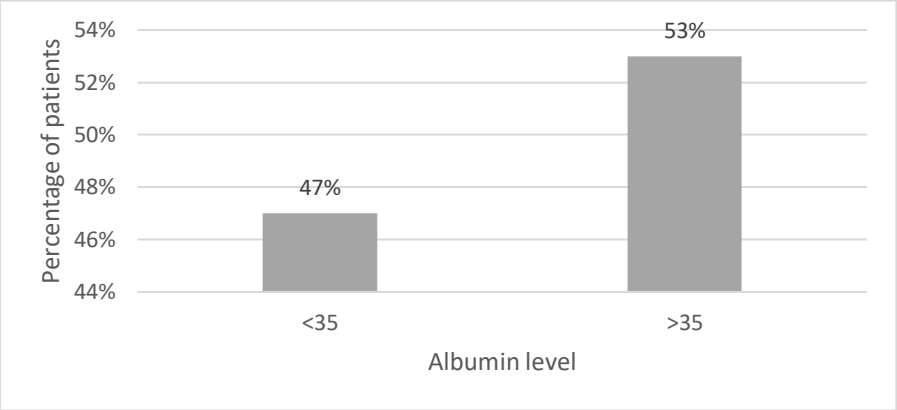

Figure N°08 : Distribution of patients according to albumin dosage (g/l).

9. Beta-2 microglobulin

All subjects included in our study received a beta-2 microglobulin test, a significant increase was found in 35% of patients.

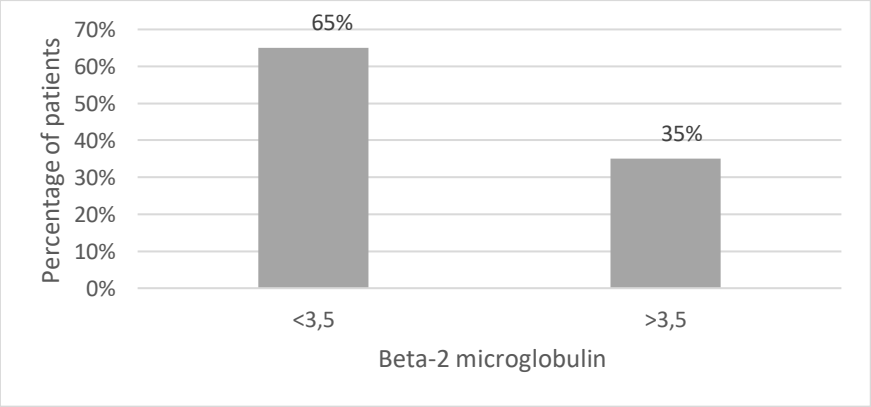

Figure N° 09 : Distribution of patients according to the dosage of Beta-2 microglobulin (mg/l)

10. Proteinuria

The 24-hour proteinuria and the urinary Bence Jones proteinuria (BJP) were tested in our patients. Proteinuria was pathological in 40% of patients, however PBJ was positive in 27% of patients.

Table 2 : Distribution of patients according to proteinuria

Proteinuria	24-hour PU (mg/24h)		PU of Bence Jones	
	<150	>150	+	-
Number of cases	60	40	27	73
Percentage (%)	60%	40%	27%	73%

11. Lactate dehydrogenase (LDH)

Lactate dehydrogenase was >200 U/L (units per litre) in 54% of patients, 15% of whom had an LDH of >460.

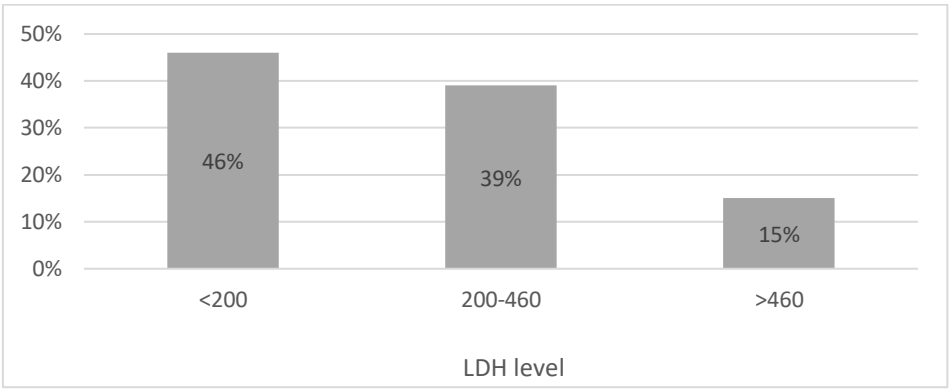

Figure N°10 : Distribution of patients according to LDH (U/L).

12. Creatinemia

Multiple myeloma patients with high creatinine levels have a worse prognosis. In this study, 27% of the patients had hypercreatinine levels (above 20mg/l).

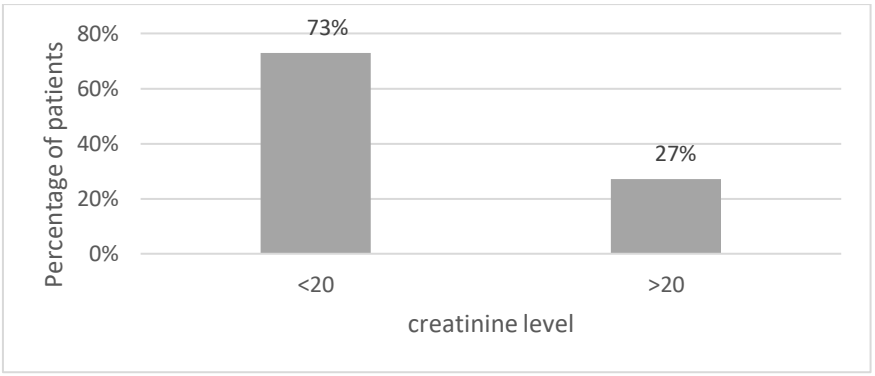

Figure N°11 : Distribution of patients according to creatinine level.

13. C-reactive protein

In our study the CRP was superior to 6mg/l in 32 patients without any infection, i.e. 32%.

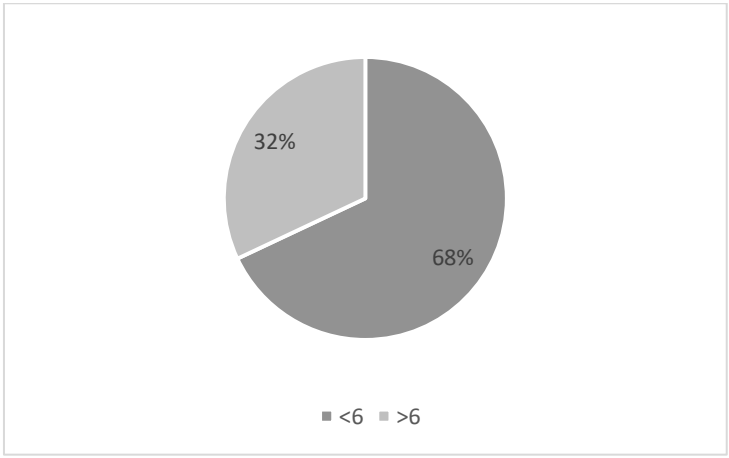

Figure N°12 : Distribution of patients according to CRP level (mg/l).

14. Sedimentation rate (SR)

Analysis of the data revealed that the sedimentation rate at the first hour was accelerated in 83% of patients.

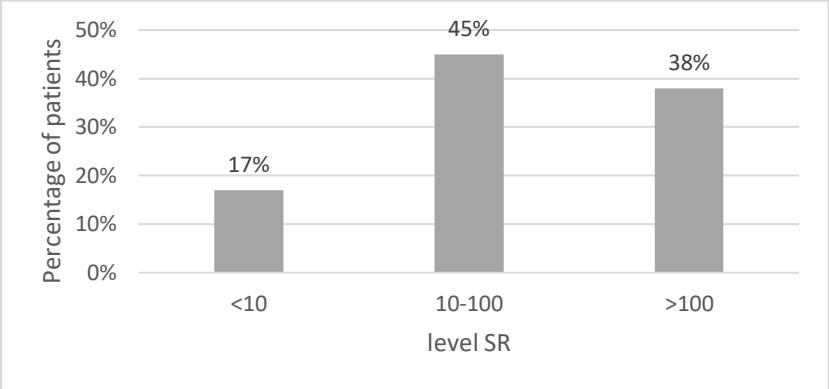

Figure N°13 : Distribution of patients according to SR (mm at 1st hour).

15. Blood count formula (FNS)

It is noted that the number of patients with a sub-standard haemoglobin (Hb) level is too high (90% of cases) and they develop normochromic anaemia. On the other, leukopenia was noted in 40% of patients. Hyperleukocytosis was noted in 20% of patients. Thrombocytopenia was observed in 40 patients (40% of cases).

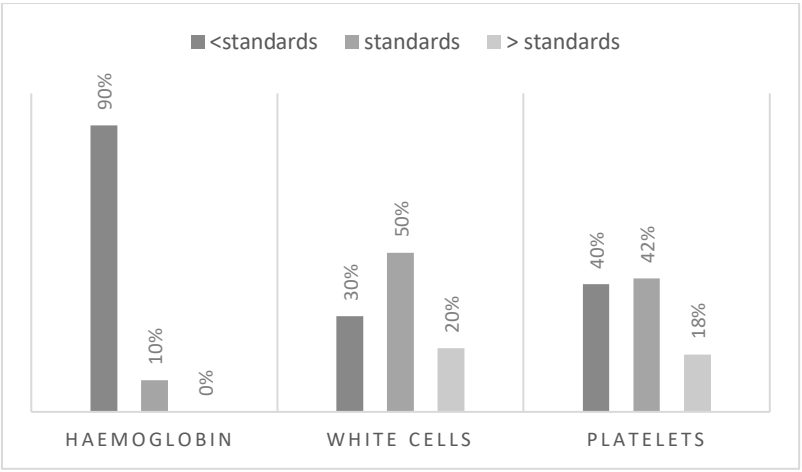

Figure N°14 : Histogram representing Hb, WBC, PLQ levels in myeloma patients.

16. Myelogram

Myelograms were performed in all our patients. It showed that 97% of the patients had abnormal plasma cell richness. Most of them are dystrophic with a plasma cell infiltration of 10-30% in 49% of patients and 30-60% in 41%. 7% have normal cell richness.

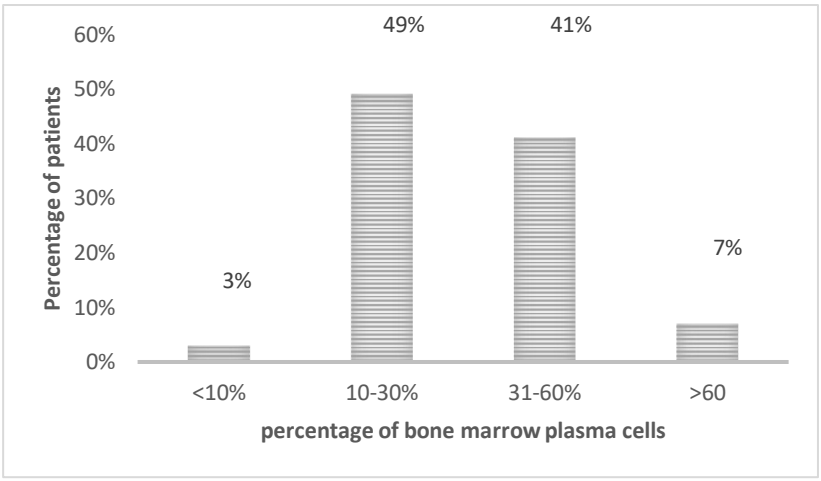

Figure N°15 : Histogram representing the distribution of patients according to the percentage of marrow plasma cells.

Discussion

Multiple myeloma accounts for about 1% of all cancers worldwide and about 2% of cancer-related mortality, Generally the frequency of incidence increases with age, the median age is 72 years but is 65 years in hospital series, the frequency of occurrence in adolescents and young adults remains exceptional **(7).** The annual prevalence in patients under 65 years of age is 64% **(4).** On the other, the results obtained by Koffi KG show that the median age is 65 years **(10).** In our series the median age of patients at diagnosis was 62 years with extremes ranging from 44 to 85 years and a peak in frequency between 61 and 70 years of age which is in accordance with the results of other studies **(11).** Multiple myeloma is more common in men than in women **(6).** In this series, the distribution of the population according to sex revealed a slight male predominance with a sex ratio of 1.13. The study conducted by Bekadja shows that the sex ratio in Algeria is 1.14 **(3).** However, our results are similar to the literature.

The circumstances of discovery in multiple myeloma are diverse, most frequently bone signs followed by predisposition to infections. The analysis of this data shows that bone pain was the main reason for consultation with a percentage of 55%. On the other hand, the frequency of infections was 36%. However, the study conducted by Koffi KG shows that infectious complications were dominated by pulmonary tuberculosis with a percentage of 67% **(10).** Also we revealed that renal involvement, asthenia and anaemia are among the tell-tale signs detected in this series, which is similar with the study by Bouatayet et al in 2012 **(12).** According to our results, hyperproteinemia was noted in 55% of all patients. According to the study realized by Nodmocrah and his team, hyperproteinemia was present in 60% of cases **(13).**

Serum protein electrophoresis represents a marker of choice for the diagnosis of multiple myeloma, our present study revealed a predominant migration of IgM in the gamma

zone followed by IgM migrating in the beta zone which is in concordance with the results obtained by Madani et al. who determined a migration in the gamma zone with a percentage of 80% **(14).** However, the study conducted by Bouferioua and his team found a monoclonal peak in the gamma globulin area with a percentage of 67.5% **(15).** Also our results are similar to those of Bouatay and Kyle's studies where a monoclonal peak was determined in 82% and 75.9% of patients respectively **(12 ; 16).** The predominance of IgG in our study (61%) is also found in the majority of works except in the study of El Mazouar where light chain myeloma was predominant **(17; 10 ; 18).** However, in our series we did not note any cases of IgE myeloma or IgD myeloma.

Protein immunofixation is an examination that makes it possible to determine the monoclonal character of the gammopathy and to determine its immunochemical type. In this series, the distribution of patients according to the type of light chain shows a predominance of the Kappa type light chain with a percentage of 66% against 34% of lambda type light chain.

The search for proteinuria is indispensable, especially in cases where the PES has only determined hypogammaglobulenemia without abnormal bands. This Bence Jones proteinuria corresponds to the presence of free light chains. In our cohort, PBJ was positive in 27% of multiple myeloma cases, the percentage we obtained is lower than that reported in other studies **(17 ; 16).**

The determination of calcemia is part of the systematic examinations for the surveillance of patients with multiple myeloma. The search for complications in our study found hypercalcaemia in 66% of our patients, which is similar to those found by Madani and colleagues **(14).** Hypoalbuminemia was found in 47% of our patients. On the other hand, the level of beta 2 microglobulin and LDH were found to be higher than normal in our patients with a percentage of 35%, 54%. Renal impairment as evidenced by a creatinine level > 20 mg/l was present in 27% of cases. These results are in accordance with the literature **(17 ; 18 ; 19).**

CRP reflects the level of interleukin 6 (IL6) **(20).** It belongs to the prognostic factors related to the intrinsic malignancy of the clone, its serum concentration is correlated with the survival and proliferative activity of myeloma cells **(21).** Our study shows that CRP was above the norm in 32% of cases.

Hematologically, the sedimentation rate (SR) is frequently elevated in the first hour; in the present study the SR was increased in 68% of patients. This result is similar to that reported by Bouferioua and his team **(15).**

In multiple myeloma, anaemia results from marrow invasion by malignant plasma cells, in this series the frequency of anaemia was 90%. However, the frequency of anaemia was estimated at 53.56% for El Mezouar and 62.5% for Bouferiouat et al in 2021 **(17; 15).**

Leukopenia and thrombocytopenia were found respectively in 30% and 40% of our patients, which is relatively similar to the results of the literature **(15).**

Cytologically, the myelogram revealed a rich marrow with more than 10% plasma cells in 90% of the patients, of which 84% had dystrophic plasma cells.These plasma cells observed had cytological criteria of malignancy, mainly multiple nuclei, central nuclei, vacuolated plasma cells, mottled plasma cells and flamed plasma cells. 7% of the patients had normal looking plasma cells. Our results are coherent with the literature **(17 ; 15).**

Conclusion

Multiple myeloma is a disease that is characterised by its polymorphism, both clinically and biologically. In this study, biological and epidemiological data on multiple myeloma were used.

Our statistical evaluations revealed that multiple myeloma is a pathology that affects elderly subjects with a certain male predominance. Furthermore, our results revealed that the majority of patients had a monoclonal peak in the gamma globulin zone followed by a peak in the beta globulin zone. In addition, hypoalbuminemia, hypercalcemia and hyperprotidemia are common in patients with multiple myeloma. In this study, the distribution of patients according to light chain type showed a predominance of Kappa light chain with a percentage of 66% against 34% of lambda light chain. On the haematological level our results revealed the presence of anaemia with a percentage of 90%. Leukopenia and thrombocytopenia were found in 30% and 40% of our patients respectively. Cytologically, the myelogram showed a rich marrow with more than 10% plasma cells in 90% of the patients, of which 84% had dystrophic plasma cells.

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Declaration of interest

No potential conflict of interest reported by the authors

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