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MULTIPLE MYELOMA: A NEPHROLOGY DEPARTMENT EXPERIENCE

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Abstract

Introduction: Multiple myeloma is defined as a malignant proliferation of a single clone of plasma cells typically accompanied by the secretion of monoclonal immunoglobulins that are detectable in the serum or urine. The most common clinical manifestations of symptomatic multiple myeloma are anaemia, infections, lytic or osteopenic bone disease, or renal failure. Renal impairment is present in 50% of patients at diagnosis and its most common cause is cast nephropathy (63 to 87%).
The aim of this study is to clarify the clinical, biological and prognosis parameters in patients with renal impairment multiple myeloma, study the different mortality factors and focus on the economic impacts that present these patients within the renal unit and hospital.
Material and Methods: This is a retrospective study of MM with renal impairment cases admitted at the nephrology department of the FEZ university hospital in a period extended from January 2010 to December 2011. The diagnosis is based on Southwest Oncology Group criteria (SWOG) and CRAB activity criteria. The outcome is evaluated according to the criteria of the International Myeloma Workings Group.
Results: Thirty two myeloma patients were enrolled for a total of 1250 admissions during a period of two years with 15 women and 17 men. The mean age is 59 ± 10 years. 81 % had impaired general condition and bone pain. 88% of cases had anemia including 1 patient with neutropenia, the acute kidney injury was found in 71%% of cases, the need for dialysis was required in 25% of patients. The monoclonal peak is observed in all patients who presented in immunofixation: Ig G 57% of cases and Ig A in 28% of cases. Monoclonal plasma cell infiltration>30% occurs in 50% of cases. The cast nephropathy myeloma is sustained in 53%% of cases. The kidney biopsy is performed in 6 patients and concluded for a myeloma tubulopathy in 2 patients and amylosis in 2 patients. All patients enrolled in our series applied for diagnosis criteria according to criteria established by SWOG in all patients. 80% of patients had bulky disease at both classifications SALMON & DURIE and ISS. 94% of our patients were treated by hydration and alkalization, only 19 % of patients received calcitonin and 53% received biphosphonates for severe hypercalcemia. 50 % of patients were proposed for ALEXANIAN Protocol; while 25% were proposed to the VAD (Vincristine-Adriamicyne-Dexametasone) protocol. Renal impairment evolution is dominated by normalization of renal function in 39% of patients. The main complication in our series is infectious one; it occurs in 53% of cases Mortality occurs in 44% of cases. The main reasons of death are neurologic complications. In univariate analyisis, the risk factors of occurring death are: elder patients > 60years, ISS stage III. 92.22% of hospitalization cost is provided by the hospital with a mean hospitalization days of 34.5 day/patient for a total of 1105 days.
Conclusion: Renal involvement in the MM is common and multifactorial, the realization of kidney biopsy is not always necessary to establish the diagnosis. Prognosis of most patients is poor due to their high tumor mass with 22, 7% of deaths. Therapies have been directed at to slow the disease progression and to prevent complications

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Introduction

Multiple myeloma is defined as a malignant proliferation of a single clone of plasma cells typically accompanied by the secretion of monoclonal immunoglobulins that are detectable in the serum or urine [1, 2]. Multiple myeloma (MM) accounts for approximately 15% of all hematologic malignancies, and around 1% of all malignancies with an annual incidence of 3-4 cases per 100,000 [3,4].

The most common clinical manifestations of symptomatic multiple myeloma are anaemia, infections, lytic orosteopenic bone disease, or renal failure, but patients with multiple myeloma might be diagnosed at an asymptomatic stage by chance[3].The only risk factor clearly identified is exposure to ionizing radiation. Agricultural occupations and exposures have been implicated [6].

Renal impairment is a common complication of MM; it is present in 50% of patients at diagnosis. Hemodialysis is required in 5 to 10% of cases. The most common cause of renal impairment is myeloma tubulopathy (63 to 87%). Light chains are freely filtered across the glomerulus and then largely reabsorbed by the proximal tubular cells.

Studies have shown that renal impairment is associated with inferior survival, and in particular, the presence of hypercalcemia and light chain proteinuria are the main causes of myeloma in more than 90% of cases. Renal failure and infection together account for the cause of death in more than half of patients with myeloma [5-8].

The aim of this study is to:

- Clarify the clinical, biological and prognosis parameters in patients with renal impairment multiple myeloma.
- Study the different mortality factors
- Focus on the economic impacts that present these patients within the renal unit and hospital.

Material and Methods

This is a retrospective study of MM with renal impairment cases admitted at the nephrology department of the FEZ university hospital in a period extended from January 2010 to December 2011.

All patients underwent radiological and biological assessment to establish diagnostic and prognosis: radiological examination by standard imaging, a serum and urine Protein electrophoresis (EP), a serum and urine immunufixation (IF), a dosing of immunoglobulin Ig (G, A, D and M), bone marrow aspiration, calcium, creatinine, 2-microglobulin and CRP.

The diagnosis is based on Southwest Oncology Group criteria (SWOG) resumed in table I.[9] and CRAB activity criteria.

CRAB activity criteria:

- Hypercalcemia >115mg/l
- Renal failure >20mg/l
- Anemia<10g/dl
- Bone disease

Renal assessment definitions:

- Acute kidney injury : serum creatinine > 15 mg / l
- Chronic kidney failure is defined by creatinine clearance <60 ml / min / 1.73 m
- Presence of tubular and / or glomerular proteinuria

Table I: Southwest Oncology Group criteria for MM Diagnosis

Major criteria	Minor criteria
Plasmocytoma on tissue biopsy	Marrow plasma cells between 10 and 30%
Monoclonal plasma cell infiltration > 30%	Monoclonal antibody Pic (IgG <35 g / L; IgA <20 g / L) and / orBence Jones proteinuria <1 g / 24 h)
Presence of serum monoclonal Ig (IgG> 35 g / L; IgA> 20 g / L)and / or urine (urinary light chain free: Bence Jones proteinuria> 1 g / 24 h without amylosis)	ostelytic bone lesions
	Decrease in Ig polyclonal less than 50% of reference intervals
The diagnosis is confirmed if associated at least one major and one minor criterion or three minor criteriaat least a + b	

The prognosis is evaluated according toISS (table III) and Salmon-Durie (table IV) system:

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Table II: International Staging System [10]

Stage I: β2 microglobulin (β2M) < 3.5 mg/L, albumin ≥ 3.5 g/dL
Stage II: β2M < 3.5 mg/L and albumin < 3.5 g/dL; or β2M 3.5–5.5 mg/L irrespective of the serum albumin
Stage III: β2M ≥ 5.5 mg/L

Table III : Durie-Salmon staging system [11]

stage I: all of - Hb > 10g/dL - normal calcium - Skeletal survey: normal or single plasmacytoma or osteoporosis - Serum paraprotein level < 5 g/dL if IgG, < 3 g/dL if IgA - Urinary light chain excretion < 4 g/24h
stage II: fulfilling the criteria of neither I nor III
stage III: one or more of - Hb < 8.5g/dL - high calcium > 12 mg/dL - Skeletal survey: Three or more lytic bone lesions - Serum paraprotein > 7g/dL if IgG, > 5 g/dL if IgA - Urinary light chain excretion > 12g/24h
Stages I, II, and III of the Durie-Salmon staging system can be divided into A or B depending on serum creatinine: - A: serum creatinine < 2 mg/dL (< 177 µmol/L) - B: serum creatinine > 2 mg/dL (> 177 µmol/L)

The outcome is evaluated according to the criteria of the International Myeloma Working Group[6].
The cost and duration of hospitalization data are collected from the information system installed since 2011 "HOSIX-NET".
Statistical analysis was performed by epidemiology laboratory and clinical research of the Medicine and Pharmacy school of Fez. We used the SPSS version 17.0 software.

Results

We have enrolled 32 myeloma patients for a total of 1250 admissions during a period of two years

General parameters

Were enrolled 15 women and 17 men with a mean age of 59 ± 10 (40-80 years). The main reason for hospitalization was bone pain in 18% of cases, acute renal injury and hypercalcemia in 15% of cases.
Impaired general condition and bone pain have been noted in 81 % of cases; anemia syndrome in 78% of cases; hyperviscisity syndrome and neurologic symptoms in both 15% of cases.

Biologic parameters

Anemia was described in 88% of cases including 1 patient with neutropenia, the acute kidney injury was found in 71%% of cases, the need for dialysis was required in 25% of patients, hypercalcemia in 64% of cases , infectious syndrome in 53% of cases and a mean proteinuria of 2.9g/day ±2.

Immunochemistry

A hyperprotidemia is found in 30 % with a mean of 70g/l (69-100g/dl). The monoclonal peak is observed in all patients who presented in immunofixation: Ig G 57% of cases, Ig A in 28% of cases, Ig M and Ig D 3% each.Monoclonal plasma cell infiltration>30% occurs in 50% of cases. The free light chain Kappa is found in 53% of cases vs 44% for Lambda. BJ proteinuria was positive in all patients and urine electrophoresis found Kappa free light chain in 44% vs 38% for Lambda.

Table IV: Biologic parameters

Blood count	N=	%
- Hemoglobin < 12g/dl	30	88%
- White blood cells	1	0.34%
- Monoclonal plasma cell infiltration>30%	16	50%
- VS>60 min	19	60%
- CRP>15 mg/l	17	53%
Chemistry	N=	%
- Albumin < 35 g/l	28	87.8%
- Monoclonal peak	32	100%
- Gama area	21	65.5%
- Beta area	13	22.3%
- Hypercalcemia (111mg/l ±21)	22	65.5%
- Acute renal injury (59g/l±28)	24	71%

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Radiology

All patients underwent to standard radiology. Bone osteolysis was found in 75%% of cases, 3 patients had a plasmacytoma.

Table V: Radiologic impairments

	N	%
Bone ostolysis	24	75%
Plasmocytoma	3	9%
Pathologic fracture	3	9%
vertebral settlement	2	7%

Renal impairment

The cast nephropathy myeloma is sustained in53%% of cases. The kidney biopsy is performed in 6 patients and concluded for a myeloma tubulopathy in 2 patients, amylosis in 2 patients. 2 biopsies were inconclusive (figure1). We sustained us nephropathy: myeloma tubulopathy in 53% of cases and glomerulopathy in 12.5% of cases which tow were amylosis. However, a functional kidney injury is observed in 34.5%; it is explained by dehydration and hypercalcemia.

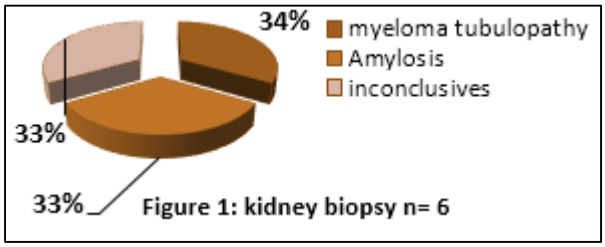


Figure 1: kidney biopsy n= 6

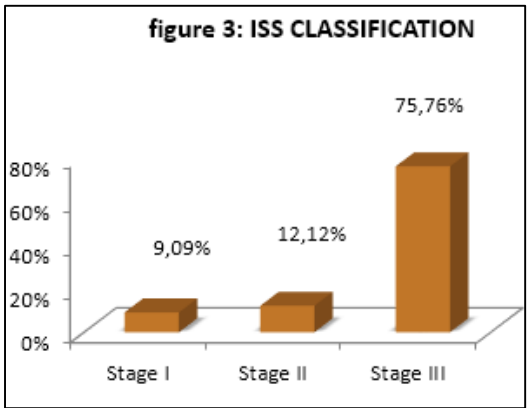
Diagnosis

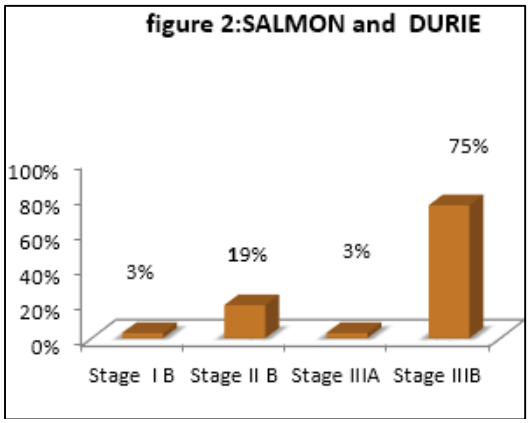
All patients enrolled in our series applied for diagnosis criteria according to criteria established by SWOG in all patients.

Treatment-Prognostic factors- Evolution

Prognosic scores

A bulky disease is noted in 80% of patients at both classifications SALMON & DURIE and ISS, 33% of patients had all CRAB activity criteria Figures (2 ,3).





Treatment

Hydration and alkalization have been applied in 94% of our patients; only 19 % of patients received calcitonin and 53% received biphosphonates for severe hypercalcemia. However, 25 % of patients underwent to hemodialysis which is 3% of cases goes on chronic hemodialysis. The hemodialysis indications were malignant hypercalcemia and advanced kidney failure. 50 % of patients were proposed for ALEXANIAN Protocol; while 25% were proposed to the VAD (Vincristine-Adriamicyne-Dexametasone) protocol.

Table VI : SYMPTOMATIC TREATEMENT

Hydratation and Alcalinisation	94 %
Calcitonine	19 %
Biphosphonate	53 %
Transfusion	47 %
Hemodialysis	25%

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Evolution

Renal impairment evolution is dominated by normalization of renal function in 39% of patients. However, 32% of patients go on evolutive chronic kidney disease (figure 4).

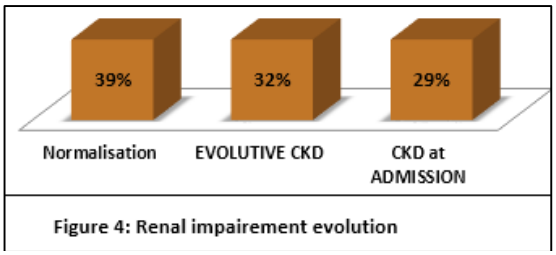

Figure 4: Renal impairement evolution

The main complication in our series is infectious one; it occurs in 53% of cases. Plasmocytoma appears in 25% of cases. Neurologic complications, hemorrhages and thrombo-embolic complications come at least respectively in 19%, 9% and 3% of cases.

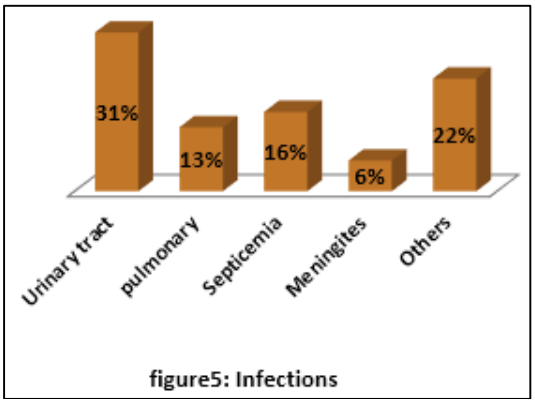

figure5: Infections

Table VII : mortality risk factors

Parameters	p
Age > 60years	**P= 0,0421**
ISS stage III	**P= 0,006**
Albumine < 30	**P= 0,08**
Infectious syndrom	NS
AKF	NS
Hemodialysis	NS
Salmon and Durie	NS
Bêta micro globine	NS

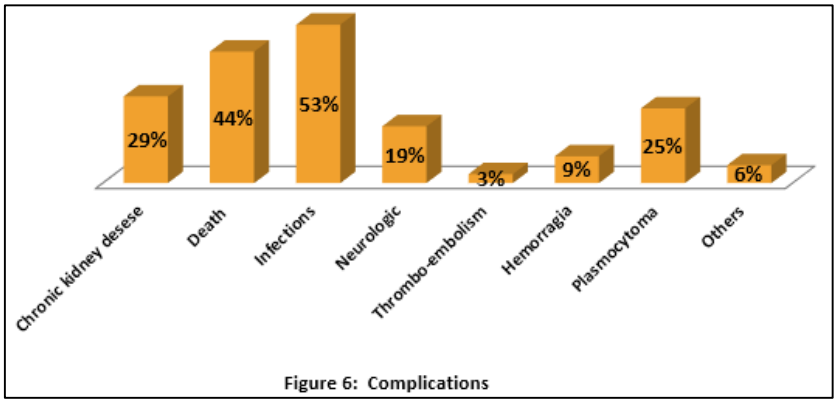

Figure 6: Complications

Mortality occurs in 44% of cases. The main reasons of death are neurologic complications, sepsis and heamorragia with respectively 28%, 22% and 22% of cases (figure 7). In univariate analyisis, the risk factors of occurring death are: elder patients > 60years, ISS stage III. Others risk factors are presented in table VI.

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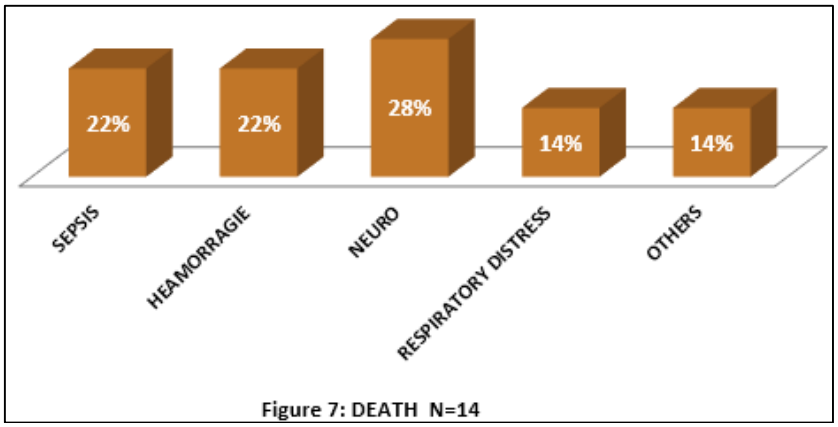

Figure 7: DEATH N=14

The treatment response criteria are determined by those established by the IMWG. In our population we got 3% of complete remission. In 19% of cases a partial remission was recorded (figure 8).

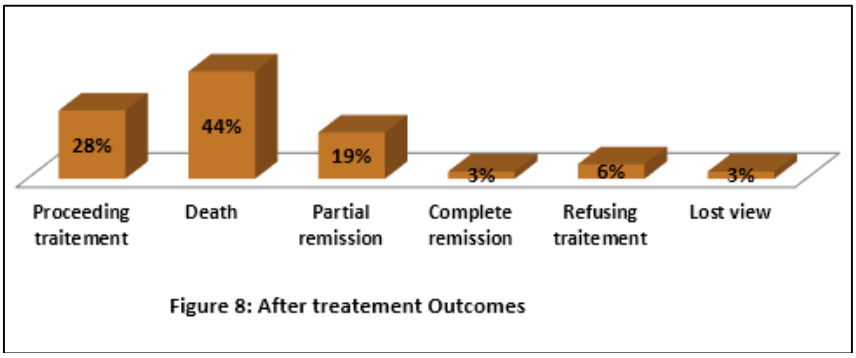

Figure 8: After treatement Outcomes

Table VIII: Economic profile

Patient number	N=32	Costs
Hospitalization days number	1105 days	34,53 day/patient
Hospitalization total cost	593 231,28 DH (€ 53 300.20)	536,88 DH (€ 48.23)
Total cost needs to be recovered by the hospital	546 998,57 DH (€ 49 146.32)	495,04 DH (€ 44.47)

536.88 DH (€ 48.23) / patient / hospitalization day

92.22% provided by hospital

The Hospitalization cost is provided in 92.22% by hospital with a mean hospitalization days of 34.5 day/patient for a total of 1105 days. It costs 536,88DH/day/patient for a total cost hospitalization of 593. 231, 28 DH (**Table VIII**).

Discussion

Multiple myeloma occurs an incurable disease even the significant progress in the management of patients with onset of newest chemotherapy drugs in last decade. It is accounts for nearly 1% of all cancers and for approximately 15% of all hematologic malignancies. The incidence of myeloma increases with age, the median age of diagnosis being 66 years old. It is very rare in individuals under the age of 40 years. Males are more commonly affected than females and the incidence in African–Americans is 2–3 times that in Caucasians. [1] Our series confirmed the literature epidemiology with a mean age of 59±10 years and men predominance (sex-ratio 1.13) [1,12].

The clinical presentation of multiple myeloma is varying and can be asymptomatic at onset. The most common clinical features reported by literature are: bone pain, osteolytic lesions, hypercalcemia and acute kidney failure. In our series, the most common symptoms at admission

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were bones pain in 81% of cases, anemia in 78% of cases and in 81% of cases patient are presenting a malignity syndrome which is concord with most literature series [1.12].

Radiological lesions and also hypercalcemia are explained by plasma cell infiltration and an imbalance between osteoclasic and osteoblastic activity. It often signals the onset of the disease and is described by several studies [13-15].

Anemia is a common consequence due to the replacement of hematopoietic tissue with tumor, to the phenomenon hemodilution related to hyperprotidémia and decrease secretion of erythropoietin in case of kidney failure. Our results are similar to those reported in other multicentric studies. However, the severity of anemia varies from study to another. Leucopenia and thrombocytopenia are rare (8-10%) but signal worse prognosis reflecting a significant tumor mass. [15-18].

Infectious syndrome is present in almost about 10% of cases at admission. It is due to humoral activation consecutive to hypogammaglobulinemia. Infection is the most common complication in our series especially urinary tract infection, septicemia and meningitis. Sedimentation rate is often high (> 50mm), this phenomenon is directly linked to the presence of the monoclonal protein [19].

The renal failure is a major evolutive complication of MM, present in approximately 20% of cases at diagnosis and in 50% of patients during the evolution. In more than two thirds of case, it is consequally due to casts precipitation formed from the interaction between monoclonal light chain and the distal tubule protein Tamm-Horsfall. The FLC are freely filtered by glomerulus and totally reabsorbed in the proximal tubule by a mechanism of endocytosis. The RF in the myeloma casts nephropathy is not only a consequence of the tubular obstruction by CL rolls, but also of the inflammatory severity [1, 6, 20]. Other reasons or renal impairment are described in tableIX.

Table IX: Renal impairment in multiple myeloma[6]

Pre-renal injury	Hypovolemia due to hypercalcemia and vomiting
Renal injury	
Tubular	Cast nephropathy
	Acute tubular necrosis
	Fanconi syndrome
Glomerular	AL Amylosis
	Randall syndrome
	Non amylosis deposit disease
	cryoglobulinemia
Post-renal injury	lithiasis

A definitive diagnosis is made by renal biopsy. A renal biopsy is especially important in patients when the clinical features or presentation may be atypical for myeloma cast nephropathy. Examples include patients with significant albuminuria, suggesting amyloid or light chain deposit disease, urinary sediment that may indicate acute tubular necrosis, or a history of allergic interstitial nephritis with an appropriate clinical picture. In the right clinical setting, a patient with a serum free light chain level greater than 1500 mg/L and low urinary albumin excretion, a presumptive diagnosis can be made without a renal biopsy[21,22].

For patients without a known diagnosis of myeloma cast nephropathy secondary to MM who are being evaluated for renal failure, a serum free light chain assay, 24-h quantification of urine total protein excretion and electrophoresis, and serum protein electrophoresis should be obtained for further evaluation. At this point, a renal service consultation would also be appropriate. In our series, nephropathy diagnosis was: casts myeloma nephropathy in 53% of cases and glomerulopathy in 12.5% of cases which tow were amylosis. Functional kidney injury is observed in 34.5% and explained by dehydration and hypercalcemia. Renal injury was observed in 15% at admission and 71% of cases occurs during evolution which joined the literature series. Hemodialysis therapy is required in 5-10% of cases. In our series, more than 20% of case underwent to hemodialysis and 3% goes in chronic hemodialysis for end renal stage disease. The development of renal failure is a negative prognostic factor for patient survival, especially if hypercalcaemia and light chain proteinuria are present. Renal failure and infection together account for the cause of death in more than half of patients with myeloma.[20-25].

Around 15 years ago, after the introduction of multiagent chemotherapy an increased rate of venous thrombo-embolism was reported. This was especially seen in patients treated with a combination of high dose dexamethasone, doxorubicin or multi agent chemotherapy and thalidomide. In subsequent studies this was also observed in patients treated with lenalidomide. The pathogenesis of the increased risk of VTE is not well understood, but several mechanisms may contribute to the development of thrombosis in MM patients. Because of this high incidence of VTE in MM patients, thromboprophylaxy is now recommended, mainly during induction treatment, but also in high risk patients on maintenance therapy. **Table (X)** resumes the imputable factor in the thromboembolic complications [26-28].

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Table X: Risk factors for venous thrombosis in multiple myeloma patients

MM related factors	Patient related factor	Treatment related factors	Procoagulation related factors
Hyper viscosity	History of VTE	Multi agent chemotherapy	High FVIII and VWF levels
Newly diagnosed disease	Immobility	Use of Thalidomide,	High P-Selectin levels
Renal failure	High age	Lenaledomide, Pomalidomide	Increased fibrinogen
CRP	Obesity	High dose Dexamethasone	Increased MP-associated
Chromosome11	Paraplegia	Recombinant erythropoietin	tissue factor activity
abnormalities	Genetic		Hypofibrinolysis
light-chain-disease	predisposition		Acquired protein C resistance
			Decreased protein S levels

The major neurological impairment in myeloma remains central cord injury, usually by compression linked to a vertebral fracture but also an epidural tumor or a plasmacytoma. It's about a Spinal syndrome, radicular syndrome with a lesional and a sub-lesional syndrome. The spinal MRI is the examination of choice to confirm the diagnosis, establish etiology and help the therapeutic decision. The peripheral nerve lesions are not to neglect because to their high incidence, morbidity and their irreversibility [6, 29].

The MM diagnosis is based on 3 points [5, 6, 15]:

1. Assessment of the medullar plasmocytosis by myelogram or bone marrow biopsy which indicate not only the plasma cells infiltration but also its dysmorphic character. In our series, Monoclonal plasma cell infiltration>30% occurs in 50% of cases vs 70% in Bouatay and al study.
2. Assessment of monoclonal component:

- Serum protein electrophoresis highlight on monoclonal character and its quantification. All our patients had monoclonal peak. However, it was observed in 65% of cases in gamma area.
- Serum protein immune-fixation: the monoclonal Ig G component is the most frequently founded in our series (57% of cases) which is similar to its frequency in other trials in literature. The free light chain Kappa is found in 53% of cases vs 44% for Lambda. However, none of our patients had a serum assay of kappa and Lambda.

3. 24-hour urine protein electrophoresis and immunofixation: BJ proteinuria was positive in all patients and urine electrophoresis found Kappa free light chain in 44% vs 38% for Lambda. Symptomatic character of myeloma is defined by CRAB activity criteria. These criterions define organ damages. 30% our patients had all CRAB criteria. Only symptomatic MM justifies the establishment of a specific treatment.

Multiple factors are incriminated in the prognosis of patients with multiple myeloma. It can be attributed to the stage and biology of the disease. Patient factors and responsiveness to therapy are also key prognostic factors (**table XI**)[30,31].

Table XI :Prognosis factors in multiple myeloma

Independent factors
- Salmon-Durie stages
- ISS stages
- Performance status≥3
- Caryotype : deletion 13 or hypodiploidy
- Translocation t(4.14) t(14.16) or deletion 17p
- LDH
- Circulating plasmocyts
Supplementary factors
- Age> 70 years
- CRP
- Creatinine >20 mg/l
- thrombopenia <15000/mm3

The prognostic assessment of the MM must be made by both the ISS and Salmon-Durie classification. Beta 2-microglobulin and albumin rate are used to define the International Staging System (ISS) (table XII), it's including also cytogenetic analysis by FISH plasma cells which it was not available at the time of this study. The ISS Consensus states that the criteria are evaluable only in symptomatic myeloma[6]. More than 75% of our patients have been admitted with a high tumor mass (Salmon-Durie stage III and an ISS stage III).

Table XII: Definition of the stages of the International Staging System (ISS) and their survival impact

Stage	Definition	Survival
I	Beta 2m< 3,5 mg/L and albumin ≥35 g/L	62 months
II		44 months
III	No I, No III Beta 2m>5,5 mg/L	29 months

Treatment of severe hypercalcemia and hypovolemia in multiple myeloma includes volume repletion, the use of calcium-lowering agents, as well as treatment of the myeloma itself. Hypercalcemia induced urinary salt wasting and can lead to intravascular volume depletion and renal function deterioration. Volume repletion with isotonic saline, if there is no underlying cardiac or

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renal disease, should be given at a rate of 200–300 ml/h and then adjusted to maintain the urine output at 100–150 ml/h. A loop diuretic such as furosemide may be used as needed. Other treatments are concurrently used to normalize calcium concentration.[18] such calcitonin which decrease serum calcium by increasing its renal excretion and by decreasing bone resorption.[19,20]. However, it is only effective for the first 48 hours [20–23]. Bisphosphonates provide a more sustained effect on the serum calcium. Their maximum effect, however, occurs in 2-4 days. Among the currently available bisphosphonates, intravenous Zoledronic acid or Pamidronate are the bisphosphonates of choice. However, Zoledronic acid is not recommended for use in patients with severe renal Impairment. Dialysis is considered as a last resort for treatment of hypercalcemia. Dialysis may be indicated in patients with severe malignancy-associated hypercalcemia andin patients who cannot be adequately hydratedsecondary to heart failure or renal insufficiency [1].

Plasmapheresis [11, 32, 35]has been shown to be a reasonable option for individuals with AKI due to cast nephropathy. It should be considered in patients with proven cast nephropathy on biopsy or in cases of high clinical suspicion in the setting of high levels of monoclonal light chains. Recently, it has been showen that the use of a new Generation dialysis membrane with high permeability (Gambro HCO 1100) could reduce the free light chain concentration (35a 70% in two hours) in patients with a MM and a renal injury requiring dialysis.

High-dose dexamethasone therapies are highly active in myeloma patients with renal impairment. Available data support the safety and efficacy of bortezomib based therapies in this setting, so bortezomib with dexamethasone is the recommended treatment for myeloma patients with renal impairment of any grade. Lenalidomide is a feasible and effective treatment option for patients with mild to moderate renal impairment, but it should be administered at the recommended reduced dose based on renal function. Thalidomide is also an option for patients with severe renal impairment, although the data on this are less extensive. Combinations of bortezomib and immunomodulatory drugs along with high-dose dexamethasone have also shown superior anti myeloma activity to the traditional vincristine/adriamycin/dexamethaxone infusion; although no comparative studies have been performed specifically in patients with renal impairment. High-dose therapy with hematopoietic stem cell transplantation (ASCT) can be an option for such patients; the high-dose regimen should consist of melphalan 140 mg/m2, and the procedure should be restricted to patients younger than 65 years of age with chemosensitive disease and a good performance status. [36-41].

Until recently, the median survival time of MM patients with renal insufficiency was less than 1 year, and patients requiring dialysis had a particularly poor prognosis. However, the prognosis for these patients has improved recently due to the availability of more effective treatments for myeloma and improvement in supportive care [42-44].

Table XIII: Dosing new drugs in renal insufficiency patients [20]

Bortezomib	1.3 mg/m2 iv j1,j4,j8,j11 No adaptation To administrate after dialysis
Thalidomide	100-200mg j1 to j28 Do not exceed 200mg Monitoring potassium
Lenalidomid	Clcr> 50 mL/min : 25 mg/j j1 toj21 Clcr 30 -50 mL/min : 10 mg/j j1 to j21 Clcr< 30 mL/min : 15 mg/48 h j1 to j21 Dialysis : 5 mg/j j1 toj21 after hemodialysis
Clcr : Creatinine clearance	

Conclusion

Renal involvement in the MM is common and multifactorial, the realization of kidney biopsy is not always necessary to establish the diagnosis. Prognosis of most patients is poor due to their high tumor mass with 22, 7% of deaths. Therapies have been directed at to slow the disease progression and to prevent complications. It is very important to be mindful of the renal associations and their consequences in multiplemyeloma in order to fully treat patients and reduce its inherent morbidity and mortality.

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