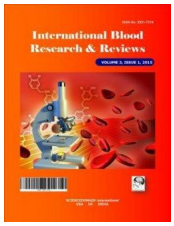

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Epidemiological and Biological Parameters of Monoclonal Plasma Cell Dyscrasias in Thirty One Patients Consulting a Moroccan Pasteur Institute

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Authors' contributions

This work was carried out in collaboration between both authors. Author IZ designed the study, collected the data, interpreted results and wrote the first draft of the manuscript. Author AB planned the study, supervised the work and critically revised the manuscript for important intellectual content. Both authors read and approved the final manuscript.

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ABSTRACT

Aims: To describe epidemiological and biological features of patients with monoclonal plasma cell dyscrasias. The patients were seen at the Moroccan Pasteur Institute in Casablanca during a period of two years and four months.
Place and Duration of Study: Laboratory of immunochemistry, Pasteur institute, Casablanca, Morocco. From April 2006 to July 2006.
Methodology: Thirty one case notes of patients who had a serum or urine monoclonal gamma or beta globulin spike were assessed.
Results: The mean age of the patients was 54.7±10.7 years (range, 26–72 years) and there were more females with a sex ratio 0.82. 66.7% of the patients had a monoclonal gamma globulin peak revealed by electrophoresis. According the results of performed agar gel immuno-electrophoresis,

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48% of them had monoclonal immunoglobulin G (IgG) antibodies, followed by class IgA with 29% of cases. Moreover, 55% of the patients were Kappa-chain positive, while 45% were Lambda-chain positive. Assessment of prognostic factors of some patients demonstrated an increased erythrocyte serum rate (66.7% of cases), anemia (50% of cases), a raised of calcium serum levels (37.5% of cases) and β2-microglobulin serum levels were higher than 3.5 mg/l (33.3% of cases). In addition, the mean concentration of proteins was 91 g/l (58.6% of cases), low levels of albumin below 36 g/l were observed (63% of cases) and the monoclonal component levels were above 30 g/l (55.6% of cases).

Conclusion: Some of our records were different from those of other series: our patients were younger with a slight predominance of female individuals. Others were consistent mainly with the more frequently observed monoclonal gamma-globulin peak, and also with the assessed levels of IgG, which is known as the most common isotype in plasma cell disorders. On the other hand, a rise of prognostic factors levels was also noted except for C-reactive protein. Nevertheless, our study pointed out that the majority of patients didn't have a rigorous monitoring of their disorders by carrying out hematological and serological examinations.

Keywords: Plasma cell dyscrasias; electrophoresis; immuno-electrophoresis; prognostic factors.

ABBREVIATIONS

PCD: Plasma Cell Dyscrasias, MM: Multiple Myeloma, WM: Waldenström Macroglobulinemia, MGUS: Monoclonal Gammopathy of Undetermined Significance, CLL: Chronic Lymphocytic Leukemia CRP: C-reactive protein, Ig: Immunoglobulin, β2-m: beta-2-microglobulin.

1. INTRODUCTION

Plasma cell dyscrasias (PCDs) are a variety of disorders characterized by monoclonal proliferation and accumulation of lymphoplasmacytic cells in the bone marrow and, sometimes, with a tissue deposition of monoclonal immunoglobulins or their components [1]. These disorders include a wide range of hematological conditions ranging from benign disorders such as monoclonal gammopathy of undetermined significance (MGUS) to malignant pathologies for example, multiple myeloma (MM), smoldering multiple myeloma (SMM), Waldenström macroglobulinemia (WM), amyloid light-chain (AL) amyloidosis, POEMS syndrome, non-Hodgkin lymphoma (NHL) and B-cell chronic lymphocytic leukemia (B-CLL) [1-3].

These diseases may be difficult to diagnose because they affect many tissues and exhibit generally non-specific symptoms [4]. Thus, the bases of the diagnosis are the presence of bone marrow plasmacytosis and the detection of an abnormal monoclonal paraprotein in the serum and/or urine, by means of electrophoresis and immuno-electrophoresis [2]. Since then, the definitive diagnoses of PCDs require a multidisciplinary approach including clinical assessment, radiology and clinical laboratory assays [4]. Furthermore, plasma cell labeling index, karyotypic abnormalities molecular alterations, analysis of beta-2-microglobulin and C-reactive protein levels are laboratory prognostic parameters, related to the intrinsic malignancy of the plasma cells, which indicate the risk of transformation from benign to malignant forms, and, therefore designate the follow-up and treatment of each individual patient [5].

In the current retrospective study, we reviewed the epidemiological and biological features of patients with plasma cell dyscrasias, established during the period between January 2004 and April 2006 in the Moroccan Pasteur Institute (Casablanca).

2. MATERIALS AND METHODS

2.1 Study Location and Patients

This retrospective study was conducted at Pasteur Institute, Casablanca, Morocco, by reviewing case notes of patients consulting immunochemistry laboratory during the period from 1 January 2004 to 30 April 2006.

This laboratory received requests for urine or serum protein electrophoresis and immuno-electrophoresis for various diseases: myeloma, immune deficiencies, hepatic insufficiency, systemic diseases and rheumatology, etc.

One of the first steps in the laboratory evaluation of a patient with a suspected PCD has been electrophoresis of serum or urine. Thus, only patients who had a gamma or beta (rarely alpha 2) monoclonal peak and a monoclonal immunoglobulin demonstrated by urine or serum protein electrophoresis and immuno-electrophoresis, respectively, were retained.

During the period of study, 1758 electrophoreses and 99 immuno-electrophoreses were gathered.

Any double immuno-electrophoresis or non-coupled to electrophoresis was excluded. Thus, our population was limited to 31 patients. Their distribution was done by taking in consideration the age, sex, nature of spike, as well as the type of immunoglobulin heavy and light chains.

Moreover, to detect whether patients had followed-up the evolution of their diseases, some prognostic factors were also evaluated such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum levels of calcium, β2-microglobulin (β2-m), hemoglobin and some other proteins.

It should be noted that bone marrow biopsies were performed in the clinic that sent the patients' sera for testing in the laboratory. We didn't get the results of these analyses.

Statistical analysis was performed by calculation of percentages and arithmetic averages.

3. RESULTS

Our current investigation was a retrospective study that included 31 Moroccan patients having a risk to develop plasma cell dyscrasias consulting Pasteur Institute, Casablanca, between January 2004 and April 2006.

Detailed epidemiological and clinical characteristics of 31 patients are shown in Table 1.

3.1 Epidemiological Data

The mean age was 54.7±10.7 years with extremes ranging from 26 to 72 years. Fifty-five percent of the patients were female and forty-five were male with a sex ratio 0.82.

The two third of our study population were located in the range between 40 and 60 years with equality of reaching for both sexes. However, a female predominance in patients over 60 years was observed. It's noteworthy to mention that the data about the age of one patient had not been found.

3.2 Immunochemical Data

According to the electrophoresis results, 66.7% of patients had a gamma-globulin monoclonal peak, against 33.3% had a monoclonal peak in beta-globulin zone.

The data from immuno-electrophoresis confirmed that the tested population in the current study had a monoclonal band in serum. In fact, we found that immunoglobulin G monoclonal antibody (Ig G) was placed in the forefront. It was observed in 15 patients (48%), Ig A was found in the second place with 9 cases (29%) followed by 4 patients (13%), who had free light-chains and 3 patients (10%) had Ig M, while in none of them Ig D and Ig E were detected (Fig. 1).

Besides that, 17 of the patients (55%) were Kappa-chain positive and 14 (45%) were Lambda-chain positive.

3.3 Biological Data

In some patients, prognostic factors as ESR, CRP, serum levels of calcium, β2-microglobulin, hemoglobin and other proteins, were also taken in consideration. According the data in Table 2, the majority of patients didn't follow-up the progression of their malignant disorders by biological tests.

Nevertheless, patients requesting for these analyzes demonstrated an elevation of ESR (66.7% of cases), anemia (50% of cases), a raised of serum level of calcium (37.5% of cases) and β2-microglobulin serum level was greater than 3.5 mg/l (33.3% of cases). Moreover, the mean concentration of proteins was 91 g/l ranged in values varying from 58 to 121 g/l (normal values of serum proteins are between 60 and 80 g/l). It was noted that serum protein electrophoresis had been performed only for 29 patients, while the others had urine electrophoresis. Thus, we found that 58.6% of patients had a hyperproteinemia against 38% having normal levels of serum proteins, whereas 3.4% of cases having a hypoproteinemia, corresponding to a patient with a monoclonal light Lambda chain.

Table 1. Epidemiological and clinical characteristics of 31 patients

P	A	S	Type of protein ep and iep	M. Ig type	Proteins Level (g/l)	Protein fractions levels (g/L):					ESR (mm)		Levels of:			
						Al	A1	A2	B	G	FH	SH	CRP (mg/l)	Hg (g/dl)	ß2m (mg/l)	Ca (mmol/l)
1	45	M	ser prot	IgM/K	90	33.12	3.96	8.82	29.52	14.58	NP	NP	NP	NP	NP	NP
2	55	M	ser prot	IgG/L	80	40.64	2.65	10.08	11.84	14.88	10	22	<6	14.6	1.56	2.35
3	60	F	ser prot	IgM/K	110	41.25	2.86	8.8	8.47	48.62	NP	NP	NP	NP	1.31	NP
4	46	F	ur prot	LLC	0.4	-	-	-	-	-	NP	NP	NP	NP	NP	NP
5	57	M	ser prot	IgA/K	76	37.012	2.356	7.524	23.408	5.7	NP	NP	NP	NP	NP	NP
6	59	F	ser prot	IgG/K	106	NF	NF	NF	NF	NF	NP	NP	NP	NP	NP	NP
7	50	F	ser prot	IgG/L	84	38,163	2.772	9.072	8.148	25.878	64	105	NP	12.8	1.05	2.24
8	71	M	ser prot	IgG/L	80	23.2	4.16	14.88	3.68	34.08	NP	NP	NP	NP	NP	NP
9	56	F	ser prot	IgG/L	84	39.06	2.856	9.576	8.232	24.276	26	54	NP	11.6	NP	NP
10	61	F	ser prot	IgG/L	120	30.72	2.4	6.96	5.28	74.64	NP	NP	NP	NP	NP	NP
11	NF	M	ser prot	IgG/L	120	34.92	2.88	7.56	6.96	67.68	NP	NP	NP	NP	NP	NP
12	52	M	ur prot	IgG/K	2	-	-	-	-	-	NP	NP	NP	NP	NP	NP
13	56	M	ser prot	IgG/L	80	36.24	3.12	12.88	13.04	14.72	8	18	<6	11.5	1.56	2.3
14	50	F	ser prot	IgA/K	116	29	1.6	5.68	3.9	74	NP	NP	NP	NP	7.76	NP
15	63	F	ser prot	LLC	72	36.43	3.24	12.96	11.304	8.064	NP	NP	<6	12.4	NP	2.54
16	72	F	ur prot	KLC	1.85	-	-	-	-	-						
			ser prot	KLC	70	35.42	3.08	13.44	9.31	8.75	42	80	<6	NP	14.16	NP
17	49	M	ser prot	IgG/K	94	36.472	3.478	10.81	9.776	33.464	NP	NP	NP	NP	NP	NP
18	67	F	ser prot	IgA/L	120	29.64	3.12	4.44	80.04	2.76	NP	NP	NP	NP	7.98	NP
19	71	M	ser prot	LLC	58	32.712	3.306	7.424	9.744	4.814	NP	NP	NP	7.9	NP	NP
20	54	F	ser prot	IgA/K	110	26.29	2.09	7.04	9.13	65.45	NP	NP	NP	6.4	2.25	NP
21	45	M	ser prot	IgA/L	90	41.58	3.42	10.89	9.45	24.66	NP	NP	NP	NP	NP	NP
22	66	F	ser prot	IgM/K	74	30.118	2.738	7.844	19.092	14.208	NP	NP	NP	NP	NP	NP
23	30	F	ser prot	IgG/K	102	31.212	2.652	6.834	8.772	52.53	NP	NP	NP	10.8	NP	NP
24	58	M	ser prot	IgG/K	80	31.28	4.08	9.2	8.72	26.72	81	115	NP	10.8	NP	NP
25	45	F	ser prot	IgA/K	72	37.152	2.52	7.92	9	15.408	105	132	NP	9.6	NP	NP
26	51	F	ser prot	IgG/L	74	33.152	2.738	9.102	8.51	20.498	64	105	NP	12.3	1.05	2.24
27	59	M	ser prot	IgA/K	96	35.424	2.016	6.528	49.344	2.688	NP	NP	NP	NP	6.77	2.65
28	44	F	ser prot	IgG/K	106	29.468	3.922	12.508	6.996	53.106	NP	NP	NP	NP	NP	2.92
29	57	M	ser prot	IgG/L	70	30.87	4.2	12.11	9.94	12.88	10	22	<6	14.2	1.56	2.35
30	66	F	ser prot	IgA/K	84	33.768	2.268	8.4	31.08	8.484	NP	NP	NP	NP	1.07	NP
31	26	M	ser prot	IgA/K	121	NF	NF	NF	NF	NF	NP	NP	NP	NP	NP	NP

P: patient; A: age; S: sex; Ep: electrophoresis; IEP: immuno- electrophoresis; M: monoclonal; Ig: immunoglobulin; Al: albumin; A1: alpha 1; A2: alpha 2; B: beta; G: gamma; ESR: Erythrocyte sedimentation rate; FH: first hour; SH: second hour; CRP: C-reactive protein ; Hg: Hemoglobin; ß2m: ß2-microglobulin; Ca: serum calcium; Ser prot: serum protein; Ur prot: urine protein; M: male; F: female; K: kappa; L: Lambda; LLC: Lambda light chain; KLC: Kappa light chain; NP: not performed; NF: not found

Table 2. Number and percentage of patients requesting for prognostic analyzes

Prognosis factor	Erythrocyte serum rate	CRP	Level of:		
			Calcium	β2-microglobulin	Hemoglobin
Number of patients who requested for each analysis divided by total number of the studied population (%)	9/31 (29%)	5/31 (16.1%)	8/31 (25.8%)	12/31 (38.7%)	12/31 (38.7%)
Number of patients having anomalies in analysis divided by number of patients requesting for prognostic factors (%).	6/9 (66.7%)	0/5 (0%)	3/8 (37.5%)	4/12 (33.3%)	6/12 (50%)

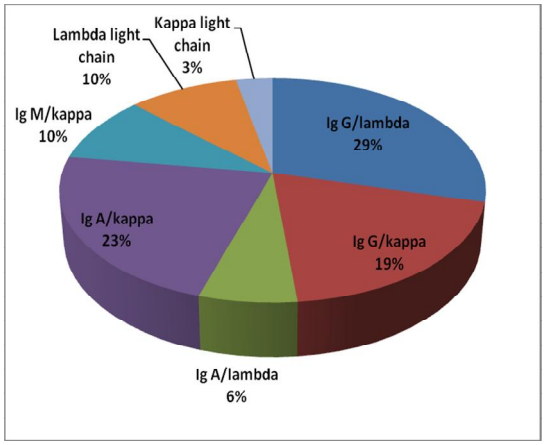

Fig. 1. Percentage of different immunoglobulin subtypes of monoclonal plasmaproliferative disorders (n=31)

With respect to the spike size, 44.4% of the cases were below 30 g/l, and 55.6% above 30 g/l, respectively. The mean concentration of the monoclonal component was 37 g/l.

On the other hand, the average level of albumin was 33.86 g/l with extremes ranging from 23.2 g/l and 41.58 g/l.

In seventeen patients (63%) having low levels of albumin, 15 patients had higher serum monoclonal protein levels. The remaining two patients had normal concentrations of beta- or gamma- globulin fractions, which were probably associated with light chain PCD. However, there was a moderate negative correlation between low levels of albumin and higher serum monoclonal protein concentrations (Pearson's correlation, r = -0.37, n = 17, p=0.12).

4. DISCUSSION

The presented investigation was the first study conducted in 2006 at Pasteur Institute in Casablanca (Morocco) aimed to highlight the epidemiological and biological features of thirty one patients having a risk to develop plasma cell dyscrasias.

Few years later, many studies, performed in Morocco and other countries, were directed to the same target. Some of the results from those investigations were consistent with our data, but others were different. In fact, our patients were younger (54.7 years), in comparison with the data, which were reported by other surveys. Beginning with a Moroccan investigation which had been executed in Mohamed V Military Hospital of Rabat [6], the mean age was 60.21 years. In other countries, the average age was a bit closer to that found by Moroccan institutions. For instance, in India [7], Egypt [1], Tunisia [8] Lebanon [9] and Saudi Arabia [10], it was 56, 58.5, 62.7, 65 and 65.6 years, respectively. However, it was much higher in Western nations especially in Iceland [11], Spain [12] and France [13], with mean ages of 70, 73 and 79 years, respectively. The observed differences in mean ages of patients with PCD between Eastern and Western nations, may be due to the quality of life, health services and medical scientific researches, which are different in the developed and underdeveloped countries.

Besides that, our outcomes had demonstrated that 93.3% of our patients were above 40 years old, but it was important to underline that only two patients were 26 and 30 years. These results were corroborated with the study by Kassem et al. [1], who showed that 96% of patients

having PCD were the older age group. This confirmed some literature data [1,4,7,14,15], according which PCDs as MM and MGUS are diseases of older adults.

Similarly the results of other studies showed that the prevalence of PCD increased with the age [1,7,13,15-17]. Nevertheless, the main difference between the cited and our data was that we noted a slight predominance of female individuals with a sex ratio 0.82 and an equality of reaching for both sexes in patients aged between 40 and 60 years, meanwhile, other authors found that men were affected more frequently than women by PCD with different sex ratios 1.08 [11], 1.2 [13,18], 1.24 [9], 1.43 [1,10], 1.71 [8], 1.94 [14] and 2.3 [6], respectively. The established predominance in female individuals can be explained by the eventual influence of geographical distribution of Casablanca population, which was presented by 50.7% of females and 49.3% of males according to 2005 and 2006 statistics performed in Casablanca [19].

On the other hand, the most frequent type of immunoglobulin in the current study was IgG. It was found in 48% of patients, followed by Ig A (29%), monoclonal light chains (13%), and the isotype Ig M (10%) which came in the last place. This distribution coincided with that reported by the clinical oncology department of Cairo University (Egypt) [1], not in point of view the percentage, but the order. In the latter inquiry, 63.6% of the patients were assessed with prevalence of IgG against 17.5% of IgA, while 13.4% had monoclonal light-chains and 5.5% had an Ig M monoclonal band. Nonetheless, our findings were not in concord with those reported by French studies [13]. Effectively, the first investigation was led in internal medicine department of Rennes university hospital [13], which revealed that isotypes repartition was: Ig G (42.8%), Ig M (31.9%), Ig A (8.9%), biclonal gammopathy (9.8%) and monoclonal light chains (6.6%), respectively. Whereas, the second research, conducted in all the department s of General Hospital of Blois [13], showed that this distribution was Ig G (59.7%), Ig M (27.5%), Ig A (11.8%) and monoclonal light chains (2.7%), respectively. In contrast, no monoclonal light chain was detected in an Indian investigation [18], while in Singh et al. survey [7], no IgM type paraprotein was observed.

Moreover, electrophoresis showed a monoclonal peak in gamma globulin fraction in 66.7% of the patients. Our current findings were in agreement with those previously reported [8,18,20], outlining a monoclonal spike in the gamma zone in 78%, 84.8% and 85.5% of cases, respectively. These observations could be explained by the fact that the gamma fraction contains the largest portion of immunoglobulins. Therefore, PCDs are the most frequently encountered in this portion of the electrophoresis. Additionally, since most IgG monoclonal proteins are cationic, they migrate to the gamma zone of the electrophoretic gel [21]. This statement may justify the predominance of the isotype IgG in all the studies, discussed above.

In addition, the association of IgG with the lambda light chain was established in 29% of cases. In the opposite, the study of Dasse et al. [22] conducted in Abidjan (Ivory Coast), indicated that the association Ig G/kappa was the most found monoclonal form in 60% of cases.

Alternatively, analysis of the association between heavy and light chains revealed that kappa light chain was more linked than was lambda light chain (55% against 45%, respectively). This statement joined the outcomes of many researches [1,7,20,22].

In this series of 31 patients, all the detected heavy chains were associated to light chains (intact immunoglobulin). This result was compatible with the data presented by Dasse et al. [22]. Nevertheless, the presence of immunoglobulin free light chains had been proven in 13% of cases.

With respect to biological tests, the hyperproteinemia touched 58.6% of our patients. A similar result was obtained from the study of Gaougaou et al. [23], in which increased serum protein levels in 63% of the cases with MM have been noticed. It was pointed out that PCDs were not always related with hyperproteinemia. Indeed, cases of PCD, presented in the current investigation, indicated free light chains with normal or low levels (hypoproteinemia) of serum proteins. A similar finding was described in another study [21] reporting that the mean serum total protein concentration was significantly higher in IgG, IgA, and IgM, compared with free light chain PCDs, where this value was within normal limits. This could be explained by the effect of low molecular weight of the light-chain secreted by malignant plasma cells about 22500 Dalton versus 40000 to 70000 Dalton, which shows the variation of molecular weight of the

heavy chains. It was important to mention that 17 of 21 patients (80.9%), having total protein level above or equals to 80 g/l, had monoclonal paraprotein concentration above 20 g/l. There was a strong positive relationship between total protein level and monoclonal paraprotein concentration (Pearson's correlation, r = 0.712, n = 21, P<0.001). As was previously reported, in a study, performed by van Hoeven et al. [21], monoclonal proteins often increase serum total protein level. In fact, it was found that paraprotein levels were reflected in significantly increased mean serum total protein in IgG, IgA, and IgM [21].

An increase in β2-micro-globulin levels in 33.3% of cases was as well noted. It has already been reported that this molecule is a small membrane protein, associated with the heavy chains of class I major histocompatibility complex proteins. It's a powerful prognostic factor, correlating with the survival in monoclonal disorders [24]. Indeed, according to the results of Di Giovanni et al. [25], in the group of patients suffering from MM or WM, the mean level of the same protein has been assessed to be significantly higher than in the group with MGUS. Values above 3 mg/L were highly indicative of a neoplastic process. They were observed in all the WM patients and in greater than 90% of myeloma patients. It was noticed, in the current study, that the patients having β2-m concentrations above 5.5 mg/l, had albumin levels below or equals to 35 g/l. This finding is in keeping with a previous investigation [26], demonstrating that serum β2m values had a negative correlation with serum albumin. However, there was a weak negative correlation between albumin and β2-m serum levels (Pearson's correlation, r = -0.34, n = 12, P = 0.309). This, maybe, was due to the small number of patients carrying out the biological test β2-m. Therefore, the current data should be proven by investigating the involvement of both β2-m and albumin serum levels in PCD in a large-scale of Moroccan patients. In this series, patients had as well serum levels of monoclonal protein above 30 g/l except for one patients suffering from kappa light chain PCD. There was a strong positive association between monoclonal component (MC) above 30 g/l and serum β2m levels (Pearson's correlation, r = 0.703, n=5).Our data were in concordance with those recorded by Charafeddine et al. [9], demonstrating that β2-m levels were related to spike size. This correlation could be explained by the fact that β2-m reflects the tumor mass [24], which is detected by hyperproteinemia due to the elevation of serum monoclonal protein in beta- or gamma- globulin zone. In contrary, normal or low (hypoproteinemia) levels of proteins were associated with normal concentrations of beta- or gamma- globulin fractions in patients suffering from light chain PCD, but presenting high levels of β2-m. This result joined that reported by Charafeddine et al. [9], finding that most of the patients, diagnosed with light chain PCD had a spike size below or equals to 20 g/l.

In assessment of serum calcium levels, according to the results of the current study 37.5% of patients had hyper-calcemia, leading to an increased risk of bone lesions and collapse of the vertebral. This was supported by the deduction reached by Pagano et al. [27], who noted that 27% of patients suffering from plasma cell leukemia had an elevation in serum calcium level. Hyper-calcemia is one of the important factors besides renal insufficiency, anemia, and lytic bone lesions (CRAB criteria), that can distinguish between MM and MGUS [1,28,29], since patients with the pre-malignant plasmatic cell disorder are known by absence of hyper-calcemia [20]. However, because MGUS is a condition of the elderly, concomitant diseases can confound the distinction [30]. For instance, hypercalcemia may be caused by hyperparathyroidism that should be considered in the absence of skeletal lesions [30]. It was also made out in the current investigation that the patients with hyper-calcemia had high values of β2-m serum concentrations, albumin levels below or equals to 35 g/l and serum levels of monoclonal protein above 30 g/l, with exception of one patient, suffering from kappa light chain PCD. Statically, there was a moderate negative correlation between albumin levels and calcium concentrations (Pearson's correlation, r = -0.48, n = 8, P = 0.226).

It was also established that the emergence of anemia was more thrust. It was perceived that 50% of patients had a drop in rate of hemoglobin which may reveal the impact of the plasma cell infiltration on the bone marrow production. In other surveys [7,27,18], anemia features were also detected, but only in 48%, 25%, and 7.2% of patients, respectively. It should be noticed that our six patients with anemia might not be affected by solitary plasmacytoma. In fact, the decrease of serum hemoglobin level isn't a criterion for this disease, which is also characterized by a low serum or urinary level of monoclonal immunoglobulin [31]. In contrast, these patients could have MM or WM, for which

the anemia is a common complication [4]. In the current study, it was also observed that 4 of 6 patients with anemia had albumin levels below 35 g/l, but had variable levels of serum monoclonal paraprotein (below or above 30 g/l regardless of the immunoglobulin isotype). There was a moderate positive correlation between albumin levels and hemoglobin concentrations (Pearson's correlation, r = 0.606, n = 6). Various studies had demonstrated a positive correlation between hemoglobin and albumin levels in patients with PCD [9,17]. However, according to our investigation, these two factors might not be indicators of the increase of MC levels of non-IgM PCD. In fact, as was previously reported [20,30], anemia may be multi-factorial in the elderly. It could be caused by conditions, different from PCD, such as renal insufficiency, iron deficiency, nutritional imbalance, occult gastrointestinal bleeding, or, less frequently, myelodysplastic syndrome. On the other hand, our observation didn't corroborate with an investigation, performed by Charafeddine et al. [9], carried out in the clinical laboratory of the American University of Beirut Medical Center with 540 patients, in which low serum concentrations of hemoglobin and albumin showed significant correlation with high M spike size above 20 g/l. The difference between the two inquiries resides in the size of the population under study. Thus, our outcome should be confirmed or rejected after study the impact of prognostic factors in a large number of patients.

Furthermore, it was explored that 66.7% of our patients had a higher erythrocyte sedimentation rate (ESR). In others surveys, an elevation of this biological test was observed in all seven reported cases with plasma cell leukemia [32] and in 94.6%, 17.9%, 25.5% of patients with MM [23], MGUS and SMM [33], respectively. In the current investigation, whatever were the ESR levels, MC concentrations were lower than 30 g/L. Probably; there is no clear relationship between ESR levels and the size of MC in patients with PCD as was previously reported [33], suggesting variability in the interaction of individual MCs with red blood cells to create rouleaux formation [33]. Besides that, due to the small number of patients, we can't judge whether or not ERS is a prognostic factor for PCDs.

Unlike the study, performed by Salonen and Nikoskelainen [34], displaying elevated CRP levels in patients with hematological malignancies (around 152 mg/l), all our five patients had a normal CRP, a prognosis index, correlated with survival and activity of proliferative cells [24]. It is also an infection indicator as a cause of death in patients with PCDs [34]. Despite of this positive outcome, the majority of serological and hematological examinations allowing to patients to have a rigorous monitoring of their PCD, had not been carried out by all of them. Additionally, the differential diagnosis between different disorders may not be done. Effectively, findings of Ig M PCD, plasma cell proliferation on bone marrow biopsy and clinical findings consistent with myeloma (CRAB signs) classically distinguished the rare diagnosis of Ig M MM from the more common WM, characterized with a monoclonal Ig M and known by lymphadenopathy, organomegaly, lymphoplasmacytic lymphoma and hyper-viscosity (related to the absolute level and structure of the Ig M pentamer) [28]. Conversely, some patients may not have all of these findings. Both diseases could share clinical and biological manifestations such as hyper-viscosity, which may lead to diagnostic errors [28,35,36]. Recent advances in cytogenetic and immuno-phenotyping of bone marrow plasma cells can help further define the differences between IgM MM and WM [28,37]. Myeloma plasmatic cells lack CD19, CD45, and CD27 expressions and are positive for CD56 (75%), CD117 (30%), and CD20 (30%) according to the report of Rawstrom et al. [38], while in WM, clonal B-cells express CD19, CD20, CD45 [36]. In contrast to WM, MM is characterized by chromosome translocations, which include not only the t(11;14) but also the t(4;14) and t(14;16) located in the genes coding for immunoglobulin heavy chains [37].

Importantly, a definitive diagnostic allows the choice of the adequate treatment for each PCD by taking in consideration age, gender, race and family history.

Our study had several limitations: the laboratory data of the PCD cases were included without their clinical diagnosis (bone marrow biopsy results, radiological studies) and many factors affecting prognosis were not assessed in the univariate and multivariate analyses due to the limited number of patients. Moreover, the current study was Pasteur Institute based and thus cannot be generalized for the entire Moroccan population.

5. CONCLUSION

The purpose of the current study was to evaluate epidemiological and biological characteristics of

patients with PCD, detected by the association of electrophoresis and immuno-electrophoresis. Our data were very similar to those reported by others investigations but slightly different in the aspect of mean age and sex ratio. It is also important to mention that biological tests weren't performed by all members of our cohort, probably because of financial constraints, that limit the opportunity for monitoring of their disorders progression and response to the respective treatment.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Ethical committee of Pasteur Institute of Casablanca Morocco approved the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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