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Original Research Article

Pattern of serum protein electrophoresis and immunofixation in plasma cell disorders

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Abstract

Background: Abnormal accumulation monoclonal plasma cells in the bone marrow cause the primary characteristics of multiple myeloma. Myeloma cells produce abnormal immunoglobulin (M protein), light chain proteins (κ and λ), and other factors, such as cytokines.

Objective: To analyze the pattern of serum protein electrophoresis and immunofixation in plasma cell disorder.

Methodology: The study was conducted at central research laboratory at ESI-PGIMSR Manicktala, Kolkata. During the period of one year, Biochemical parameters and SPEP was performed for total 40 patients of plasma cell disorder diagnosed by bone marrow examination. The bone marrow aspirate and biopsy results were reviewed and the diagnosis was confirmed by doing immunofixation.

Results: Mean age of patients was 57.35 years while male to female ratio was 3:1. Globulin >5g/dL was found in 50% of pt while 70% had A/G ratio less than 1. Renal insufficiency was present in15%. M spike was present in all patients when SPEP was done; 70% was in gamma and 30% in beta region. Paraprotein heavy chain IgG was present in gamma region in 80% cases while IgA and IgM was more commonly present in beta region (60%). Mean concentration of M protein was 2.6g/dL. In 65% patients M protein was >1.0g/dL. The most frequent heavy chain paraprotein was G (75%) followed by M (15%) and A (10%). Kappa constituted 85% for light chain paraprotein. IgG-Kappa was the most commonly found paraprotein.

Conclusion: Abnormal concentrations of total serum protein, serum globulin and A/G ratio was present in >50% of patients while M spike in SPEP and M band in IF was found in all the patients. For early diagnosis patients suspected to have plasma cell myeloma the serum protein electrophoresis and immunofixation remain an easy gold standard test for cases with secretory plasma cell myeloma.

Keywords: Immunofixation, M spike, plasma cell disorder, serum protein electrophoresis.

1. Introduction

Plasma cell disorders are a spectrum of disease like multiple myeloma, MGUS, Plasmacytoma etc. Monoclonal gammopathy of undetermined significance (MGUS) is a condition that may precede multiple myeloma [1]. Patients with MGUS have monoclonal protein present without evidence of end organ damage (CRAB criteria-Calcium elevation>11mg/dL, Renal dysfunction-creatinine>2mg/dl, Anemia Hb<10g%, Bone disease-lytic lesion on radiological investigation)[2,3]. The rate of progression from MGUS to multiple myeloma is 0.5% to 1% per year [4]. Multiple myeloma is a systemic malignancy of plasma cells that typically involves multiple sites within the bone marrow that secrete all or part of a monoclonal antibody [1-4]. Plasma cell myeloma constitutes about 10% of hematologic malignancies and 1% of all malignancies [5].

More than 90% of patients present with increased (≥10%) clonal bone marrow plasma cells and circulating monoclonal proteins in serum and/or urine as measured by immunofixation or immunofixation plus serum free light chain assay [6]. Other presenting characteristics include

anemia; lytic bone lesions and pathologic fractures resulting in symptoms of bone pain; fatigue; weakness; renal insufficiency; hypercalcemia; weight loss; and paresthesias[7,8]. The most significant risk factor for multiple myeloma is age: 96% of cases are diagnosed in people older than 45 years, and more than 63% are diagnosed in people older than 65 years. Thus, it is thought that susceptibility to myeloma may increase with the aging process [9]. The median patient age at diagnosis is 69 years. Men, and patients with African heritage, are at greater risk than women and whites [10]. Other risk factors include exposure to radiation and environmental toxins, such as pesticides, herbicides, and petroleum products. Multiple myeloma may develop in individuals without these risk factors [9].

Monoclonal expansion of myeloma plasma cells within the bone marrow interferes with the production of normal blood cells. Excessive M protein causes hyper viscosity of the blood; whereas excessive light chains cause end organ damage for example renal failure. Lesions of bone are largely caused by the release of cytokines that promote bone resorption via up regulation of osteoclast activity, differentiation, and maturation osteoclast activation leads to the release of mediators that stimulate further clonal proliferation of myeloma cells and subsequent tumor growth [11]. The best method for detecting M-protein (monoclonal Protein) is high resolution agarose gel electrophoresis. M-protein is generally observed as a localized band which is frequently seen on gamma or beta globulin region, it may also be seen on Alpha 2 globulin region but this situation is very rare [12,13]. Immunofixation electrophoresis is used to identify the clonality of M-proteins observed on agarose gel electrophoresis. Bone marrow examination including aspiration and biopsy are gold standards for assessment of bone marrow infiltration by plasma cells, and to study the morphology of these cells [14]. Our study presents the patterns of serum protein electrophoresis in patients diagnosed with plasma cell myeloma by bone marrow examination.

2. Methods

The present study was conducted at Central Research Laboratory, ESI-PGIMSR, Manicktala Kolkata for a period of one year from April 2016 to March 2017. The patients with plasma cell disorder who were diagnosed by bone marrow examination considered and collected 2ml blood sample in clot vial and the serum was used for investigation. Biochemical parameters like total protein, globulin, A/G ratio, urea and creatinine were performed in automated analyzer Beckman coulter AU480 using dedicated reagents. Among special investigation SPEP and IF was performed for all patients. Electrophoresis of serum proteins was performed by high resolution Agarose gel electrophoresis in semi-automated instrument (Hydrasys from Sebia). Densitometry was performed after electrophoresis to quantify protein fractions and to detect M spike if present. The samples were further investigated by immunofixation electrophoresis with antisera to heavy chains isotypes (α, γ, μ) and light chains isotypes (λ, κ) in Hydrasys from Sebia. The subjects were explained the purpose of the study and informed consent was taken from the subjects. Ethical clearance for this study was accorded by Institutional Ethical Committee, ESI-PGIMSR, Manicktala.

3. Results

We found male to female ratio of plasma cell disorder is 3:1 and the mean age of diagnosis is 60.7 years (Table 1). In our study 50% cases had creatinine level >1.0mg/dl and 15% had >2.5%. Regarding total protein and its fraction we found total protein >10.0g/dl in 25%, albumin <4.0g/dl in 80%, globulin >5.0g/dl in75% and A/G ratio less than 1 in 70% cases (Table 2). Regarding the frequency of M- protein the most common one was IgG (75%), followed by IgM (15%), and IgA (10%); with 85% of cases had kappa and 15% had lambda light chain(Figure-1&2). M spike in gamma region was constituted by IgG in 86% cases while IgA and IgM was present only in 14% cases, on other hand m spike of beta region was contributed by IgG in only 50% cases and other 50% was contributed by IgA and IgM. As a whole the most common paraprotein was IgG (75%), followed by IgA (12.5%) and IgM (12.5%) and most common light chain was kappa (85%) followed by lambda (15%) (Table 4). The IgG κ constitute 70% which was most common type of paraprotein found. The study reports five different patterns of paraprotein fractions, the IgG κ constitute 70% which was most common, IgG λ (10%), IgM κ (10%). IgA κ (5%) and IgA λ (5%)(Figure 3). We performed densitometry after SPEP to observe various protein fraction and m spike in the present study and noted (Figure 4 & 5). All the cases showed m spike where mean concentration of m protein was 2.6mg/dl while 40% had m protein concentration > 3g/dl. M spike was present in gamma region in 70% cases and in beta region in 30% cases (Table 3).

Table 1: Demography

Age interval (in years)	Total patients in each group		Male		Female	
<45	2	5%	2	7%	0	0%
46-55	6	15%	4	13%	2	20%
56-65	20	50%	14	47%	6	60%
66-75	8	20%	6	20%	2	20%
>75	4	10%	4	13%	0	0%
	40	100%	30	100%	10	100%
Mean age in years	60.7		61.7		53	

Table 2: Biochemical Parameters

Urea mg/dl	No & % of cases	Creatine mg/dl	No & % of cases	TP g/dl	No &% of cases	Alb g/dl	No & % of cases	Glob g/dl	No & % of cases	A/G Ratio	No and % of cases
< 20	20 (50%)	<1.0	20 (50%)	< 5.0	2 (5%)	<1.0	0	<3.0	8 (20%)	<0.5	16 (40%)
21-30	10 (25%)	1.0 -1.5	10 (25%)	5.1 -7.5	12 (30%)	1.1-2.0	2 (5%)	3.1 -5.0	12 (30%)	0.6-1.0	12 (30%)
31-40	4 (10%)	1.6 – 2.0	4 (10%)	7.6 -10.0	16 (40%)	2.1-3.0	12 (30%)	5.1-7.0	12 (30%)	1.1-1.5	8 (20%)
41-50	0	2.1-2.5	2 (5%)	10.1 -12.5	8 (20%)	3.1-4.0	18 (45%)	7.1- 9.0	4 (10%)	1.6-2.0	2 (5%)
51-60	2 (5%)	2.6 -3.0	0	12.6 – 15.0	2 (5%)	4.1-5.0	8 (20%)	9.1-11.0	4 (10%)	2.1-2.5	0
>60	4 (10%)	>3.0	4 (10%)	>15	0	>5.0	0	>11.0	0	>2.5	2 (5%)

Creat = creatinine, TP = Total protein, GLOB = Globulin, ALB = albumin A/G RATIO = albumin /globulin ratio

Table 3: Quantification of M Spike in g/dL

	Interval	No	%
M band concentration (g/dL)	<1.0	14	35
	1.1-2.0	8	20
	2.1-3.0	2	5
	3.1-4.0	6	15
	4.1-5.0	4	10
	5.1-6.0	4	10
	>6.0	2	5
Mean concentration of m band (g/dL)	2.6	40	100%

Table 4: Distribution of Paraprotein Type in Gamma and Beta Region

Location of m spike	IgG		IgM		IgA		Total	
Gamma globulin	24	86%	2	7%	2	7%	28	70%
Beta globulin	6	50%	3	25%	3	25%	12	30%
Total	30	75%	5	12.5%	5	12.5%	40	100%

Figure 1: Paraprotein heavy chain type IGG, IGA and IGM in m spike

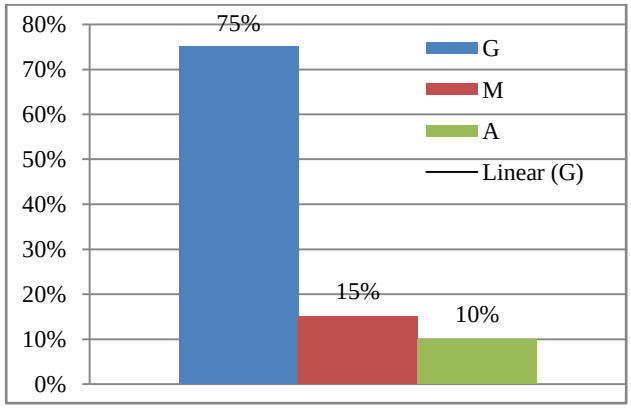


Figure 2: Paraprotein light chain type kappa and lambda

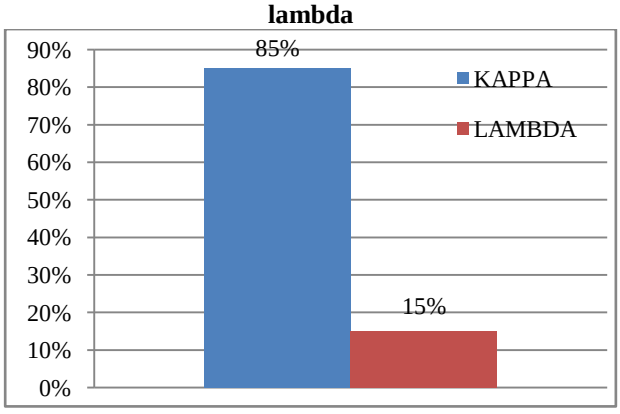


Figure 3: Paraprotein Fraction types in Immunofixation

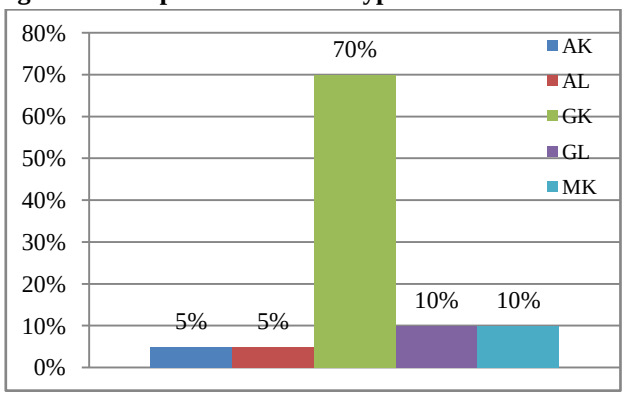


Figure 4: SPEP in Agarose Gel Electrophoresis (1-4 Samples Showing M Band&5-Control)

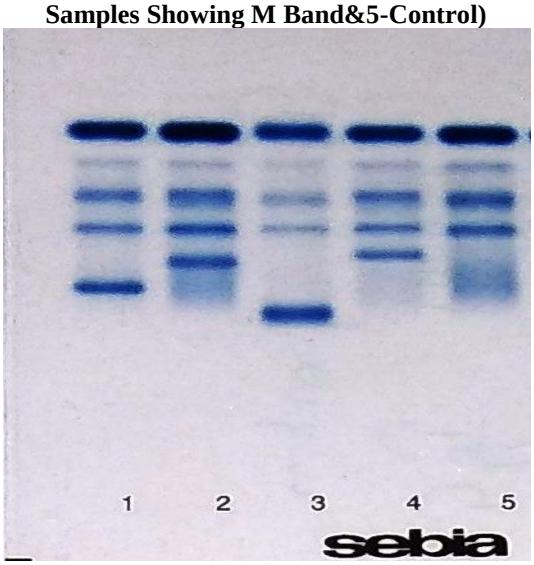


Figure 5: The Protein Fractions after performing Densitometry for Quantification of Protein Fractions and showing M spike

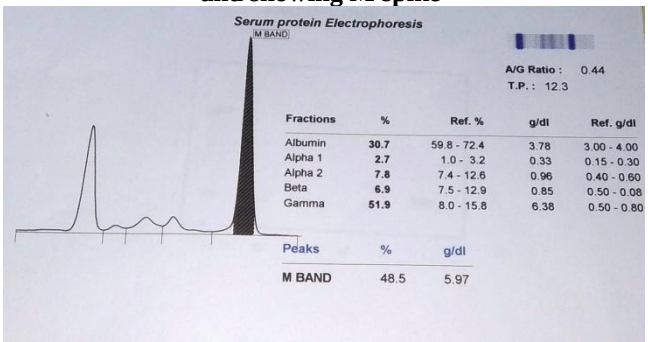
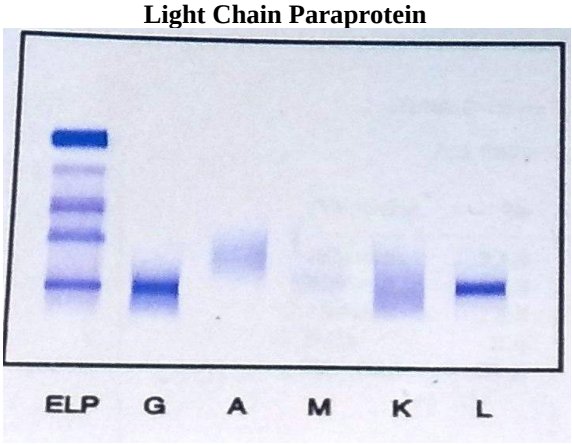


Figure 6: Immunofixation - Type of Heavy Chain and Light Chain Paraprotein



4. Discussion

Multiple myeloma is an uncommon malignancy accounting for approximately 10% of all hematological malignancies and 1% of all malignancies. Multiple myeloma arises from plasma cell dyscrasia. These malignant plasma cells synthesize monoclonal antibody and release it to the circulation. As a result high concentration of monoclonal antibodies is present in bone marrow as well as in serum [15]. Patients with plasma cell dyscrasia present a variety of symptoms such as presence of tumor, para-proteinemia (abnormal protein), osteolytic lesions, renal dysfunction, recurrent infections and hematological abnormalities, which are not specific to the disease, thus delaying the diagnosis[16,17]. The emergence of techniques likes bone marrow aspiration or biopsy (invasive); and serum protein electrophoresis (less invasive) facilitates the diagnosis and monitoring the treatment response in MM patients. Occasionally, plasma cells do not secrete any para protein; in such conditions the results of bone marrow biopsy, radiological examinations (non-invasive) and other clinical symptoms interpret MM.

We observed overall changes in the biochemical parameters and electrophoretic pattern of serum protein profile. The study included 40 cases of plasma cell disorder diagnosed by bone marrow examination (aspiration and biopsy). On analyzing we found that 80% of patients were older than 55years and male to female ratio was 3:1. Mean age was 60.7 years. As revealed by various studies, the most significant risk factor for multiple myeloma is age: 96% of cases are diagnosed in people older than 45 years, and more than 63% are diagnosed in people older than 65 years. Thus, it is thought that susceptibility to myeloma may increase with the aging process [9]. The median patient age at diagnosis is 69 years. Men, and patients with African heritage, are at greater risk than women and whites [10].

Approximately 20 to 50 percent of patients with multiple myeloma presented with an elevated serum creatinine at the time of diagnosis [18-21]. The spectrum of kidney impairment ranges from mild injury that may be rapidly reversible (e.g., volume depletion, hypercalcemia) to severe acute kidney injury (AKI) requiring hemodialysis (e.g., light chain cast nephropathy). Some patients with multiple myeloma may experience a gradual or progressive increase in serum creatinine over a period of six months or more [22].

In our study 50% patient had creatinine more than 1mg/dl and 15% patients had 2.5mg/dl or more reflecting renal compromise. The 2 major types of protein present in the serum are albumin and the globulin proteins. Albumin level is decreased, when there is less production of the protein by liver or increased loss of albumin. The reduction in albumin concentration is the most common change in the serum of MM patients [23]. In multiple myeloma the gamma globulin level is increased [24,25]. The changes in serum protein fractions reflect chiefly the reactions of the host to the presence of tumor. Our results showed significant elevated volume of gamma globulin fraction in 75% of cases and low albumin (< 4.0g/dl) in 80% cases. Normal A/G ratio is more than 1[26]. A ratio less than 1 or much greater than 1 give clues about problems in the body. Only marked changes of major constituents, such as albumin and Igs, including paraproteins are likely to alter total protein concentrations and A/G ratio significantly [27, 28]. In our study 70% patient A/G ratio was less than 1.0 and in 25% cases total protein was >10.0g/dl. SPEP measures the amount of protein fractions in the blood and finds abnormal proteins. The SPEP is broken down into the 5 following categories: Albumin, Alpha-1, Alpha-2, Beta and Gamma (Figure 2). In particular, this test can detect the presence of "M protein" another name for the large number of abnormal monoclonal antibodies being produced. The circulating M-protein may consist of an intact immunoglobulin, the light chain only, or (rarely) the heavy chain only. The heavy chain is from one of the five immunoglobulin classes G, A, M, D or E, while the light chain is either kappa or lambda in type. It occurs as intense, narrow band most often found with the gamma-globulins, then in a diminishing frequency in the b-globulin and rarely in a2 regions. Generally IgA, IgG and IgM proteins are not observed on the a2 fractions [29,30]. Very rarely, biclonal gammopathies (accounts for 1% of all monoclonal gammopathies) or triclonalgammopathy can be observed in multiple myeloma. The M protein spike is usually greater than 3-gm/dL in-patients with MM, up to 1/5th of patients with this tumor may have M protein spike of less than 1 gm/dL [31]. In our study all patients had M-band in SPEP with a mean value of the paraprotein 2.6g/dl and out of them 40% had >3 g/dl reflecting the disease severity. Much of the clinical importance is focused on the subset gamma

region of the Globulins; because, predominantly immunoglobulin migrate to this region. In multiple myeloma the gamma level is increased [32,33]. In our study the m spike was in gamma globulin region in 70% of cases while 30% was in beta region. A study conducted in India showed the presence of M-band in 87.5% and 12.5% of all cases in gamma and beta regions respectively [34]. IgG paraprotein tend to remain in gamma globulin region in most of cases while IgA and IgM have a higher tendency to migrate in beta globulin region when compared to IgG, which was also seen in a study conducted in USA [35].

Immunofixation identifies the type of immunoglobulin protein(s) present in monoclonal bandson a protein electrophoresis pattern; typically determines the presence of a heavy chain (IgG, IgM, IgA) and a light chain (kappa or lambda). Regarding the frequency of M- protein in our study the most common one was IgG (75%), followed by IgM(15%), and IgA (10%); with 85% having kappa and 15% having lambda light chain(Figure-6). Frequency rate in one study was nearly equal 75.47% for IgG, 16.98% for IgA, 64.16% for kappa, 35.84% for lambda [36]. IgG isotype and kappa light chain was the most frequent in our population, and the less frequent was IgA & IgM. However, IgM isotype was common in other populations such as France(37).We found five different patterns of paraprotein fractions, where IgG κ constituted 70% which was most common, others fraction were IgG λ (10%), IgM κ (10%). IgA κ (5%) and IgA λ (5%). Our study showed high sensitivity of serum protein electrophoresis and immunofixation in patients diagnosed with plasma cell myeloma (100%). The sensitivity was high in Netherlands (90.1%), and United State of America (94.4%).The sensitivity was higher in our study because of the fact that the number of patients reviewed was less than the other studies [38,39].

5. Conclusion

For early diagnosis of patients suspected to have plasma cell dyscrasia; the serum protein electrophoresis and immunofixation remains an easy, less invasive test with high sensitivity.

References

[1]. Kuehl WM, Bergsagel PL. Multiple myeloma: evolving genetic events and host interactions. *Nat Rev Cancer*. 2002; 2(3):175-187.

[2]. Rajkumar SV, Dimopoulos MA, Palumbo A, *et al*. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. *Lancet Oncol*. 2014; 15(12): e538-e548.

[3]. Adapted from Durie BGM. Patient Handbook. 2015 ed. International Myeloma Foundation website: http://myeloma.org/pdfs/PHB.pdf. Accessed October 1, 2015. © International Myeloma Foundation (IMF), Patient Handbook 2015, www.myeloma.org. 800-452-Cure.9)

[4]. National Cancer Institute. Plasma cell neoplasms (including multiple myeloma) treatment (PDQ®). http://www.cancer.gov/cancertopics/pdq/treatment/myeloma/healthprofessional. Accessed August 14, 2014.

[5]. Joseph RM, Craig BR, Francis KB. Management of newly diagnosed symptomatic multiple myeloma: updated mayo stratification of myeloma and risk-adapted therapy (mSMART) consensus guidelines. *Mayo Clin Proc* 2013; 88: 360-376.

[6]. Durie BGM. Concise review of the disease and treatment options: multiple myeloma cancer of the bone marrow. 2011/2012 ed. International Myeloma Foundation website. http://myeloma.org/pdfs/CR2011-Eng_b1.pdf. Accessed May 15, 2014.

[7]. Kyle RA, Rajkumar SV. Criteria for diagnosis, staging, risk stratification and response assessment of multiple myeloma. *Leukemia*. 2009; 23(1): 3-9.

[8]. Nau KC, Lewis WD. Multiple myeloma: diagnosis and treatment. *Am Fam Physician*. 2008; 78(7): 853-859.

[9]. Multiple Myeloma Research Foundation. Newly diagnosed patients: what is multiple myeloma? http://www.themmrf.org /living-with-multiple-myeloma/newly-diagnosed-patients/what-is-multiple-myeloma/. Accessed May 15, 2014.

[10]. National Cancer Institute. SEER Cancer Statistics Review 1975-2011. http://seer.cancer.gov/csr/1975_2011/results_merged/sect_01_overview.pdf.Accessed May 15, 2014.

[11]. Southerst D., Dufton J, Stern P.: Multiple myeloma presenting as sacroiliac joint pain: a case report. *J Can Chiropr Assoc.* 2012; 56: 94-101.

[12]. Kyle AR, Rajkumar SV, Lust AJ. Monoclonal gammopathy of undetermined significance and smoldering multiple myeloma. In: Greer JP, Foerster J, Lukens JN, Rodgers GM, Paraskevas F, Glader B, editors. Wintrobe's clinical hematology. Chapter 97.11th ed. Philadelphia: Lippincott Williams & Wilkins; 2004. p. 2566–7.

[13]. Longo DL. Plasma cell disorders. In: Fauci AS, Braunwald E, Isselbacher KJ, Wilson JD, Martin JB, Kasper DL, *et al*., editors. Harrison's principles of internal medicine. Vol. 1, Chapter 114. 14th ed. New York: McGraw-Hill Co; 1998. p. 712–8.

[14]. Harousseau JL, Dreyling M. Multiple myeloma: ESMO Clinical Practice Guidelines for diagnosis,

treatment and follow-up. *Annals of Oncology* 2012; 21: 155–157.

[15]. Durie BG, Salmon S. A clinical staging system for multiple myeloma: correlation of measured myeloma cell mass with presenting clinical features, response to treatment and survival. *Cancer*. 1975; 36:842–54.

[16]. Kyle, RA., Sequence of testing for monoclonal gammopathies. *Arch Pathol Lab Med* 1999; 123(2):11-48.

[17]. Munshi, NC, Immunoregulatory mechanisms in multiple myeloma. *Hematol Oncol Clin. North Am* 1997; 11:51.

[18]. Bladé J, Fernández-Llama P, Bosch F, *et al*. Renal failure in multiple myeloma: presenting features and predictors of outcome in 94 patients from a single institution. *Arch Intern Med* 1998; 158:1889.

[19]. Kyle RA, Gertz MA, Witzig TE, *et al*. Review of 1027 patients with newly diagnosed multiple myeloma. *Mayo Clin Proc* 2003; 78:21.

[20]. Knudsen LM, Hippe E, Hjorth M, *et al*. Renal function in newly diagnosed multiple myeloma--a demographic study of 1353 patients. The Nordic Myeloma Study Group. *Eur J Haematol* 1994; 53:207.

[21]. Knudsen LM, Hjorth M, Hippe E. Renal failure in multiple myeloma: reversibility and impact on the prognosis. Nordic Myeloma Study Group. *Eur J Haematol* 2000; 65:175.

[22]. Alexanian R, Barlogie B, Dixon D. Renal failure in multiple myeloma. Pathogenesis and prognostic implications. *Arch Intern Med* 1990; 150:1693.

[23]. Petermann, ML, *Med clin North AM*, 1961; 9:537-551.

[24]. George, ED., Sadovsky, R., Multiple myeloma: recognition and management. *Am Fam Physician* 1999; 59: 1885-1894.

[25]. Ravel, R., Clinical laboratory medicine: clinical application of laboratory data 6th ed. St. Louis: *Mosby*, 1995: 343-346: 350.

[26]. Dupree, Shandi. *Electrophoresis (Methods in Biochemistry)*. 1st edition. New Delhi, India: World Technologies, Publishing; 2012 Jan 1.

[27]. Fonseca R., San Miguel J.: Prognostic factors and staging in multiple myeloma. *Hematol Oncol Clin North Am*. 2007; 21:1115-40 ix.

[28]. Munshi N.C., Longo D.L., Anderson K.C.: Plasma cell disorders. In Loscalzo J., Longo D.L., Fauci A.S., Dennis L.K., Hauser S.L. Harrison's principles of internal medicine. McGraw-Hill Professional, 2011; 18th ed., Ch. 111: 936-44.

[29]. O'Connell TX, Horita TJ, Kasravi B. Understanding and interpreting serum protein electrophoresis. *Am Fam Physician*. 2005; 71:105–12.

[30]. Kyle RA, Rajkumar SV. Plasma cell disorders. In: Goldman L, Ausiello D, editors. Cecil textbook of medicine. Chapter 196. 22nd ed. Philadelphia: W. B. Saunders; 2004. p. 1184–6.

[31]. Alexanian, R., Weber, D., Liu, F., Differential diagnosis of monoclonal gammopathies. *Arch Pathol Lab Med* 1999; 123: 108- 113.

[32]. Petermann, ML, *Med Clin North AM*, 1961; 9:537-551.

[33]. Ravel, R., Clinical laboratory medicine: clinical application of laboratory data 6th ed. St. Louis: *Mosby*, 1995: 343-346,350

[34]. Sunita T. The role of Serum Protein Electrophoresis in the Detection of Multiple Myeloma: An Experience of a Corporate Hospital. *Journal of Clinical and Diagnostic Research* 2012; 6: 1458-1461.

[35]. Howard T, Chin YC, Kevin SL. Accuracy of serum IgM and IgA monoclonal protein measurements by densitometry. *Annals of Clinical & Laboratory Science* 2003; 33: 160-166.

[36]. Kalpana S, Bhawna S, Sarika A. Immunological evidence of monoclonal gammopathy in North India: a hospital based study. *Pathology and Laboratory Medicine International* 2010; 2: 107–111.

[37]. Saleun JP, Vicariot M, Deroff P, Morin JF. Monoclonal gammopathies in the adult population of Finistère, 14 France. *J Clin Pathol* 1982; 35: 63–68.

[38]. Andries JB, Ageeth BR, Coby E. Screening for M-proteinemia: serum protein electrophoresis and free light chains compared. *Clin Chem Lab Med* 2009; 47:1507–1511.

[39]. Jerry AK. Screening panels for monoclonal gammopathies: time to change. *Clin Biochem Rev* 2009; 30: 105-111.