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Monoclonal gammopathy in iran: prevalence and isotype distribution

Abstract

Background: We assessed the prevalence and isotype distribution of monoclonal gammopathy in the Noor Pathobiology laboratory of Iran.

Patients and Methods: From June 21, 2012 to June22, 2014, a total number of 18489 Iranian patients who referred to Noor Pathobiology lab were included in our study. Serum protein electrophoresis was performed on all sera. Serum sample with discrete or localized band was subjected to capillary zone electrophoresis (CZE) and immuno subtraction by Capillaries 2 instrument. Sex- and age-related prevalence rates of monoclonal gammopathy were calculated.

Results: Monoclonal gammopathy was detected in 736 of the 18489 study participants, yielding a prevalence of 3.98% in the total population screened. The prevalence in men was higher than in women. 197 samples of 736 samples were immuno typed. Isotype distribution of immuno globulins were IgG/Kappa in 33.5% (n=66) of patients, IgG/Lambda in 16.7% (n=33), IgA/Kappa in 23.3% (n=46), IgA/Lambda in 7.6% (n=15), IgM/Kappa in 7.6% (n=15), IgM/Lambda in 1% (n=2), Kappa light chain in 3.5% (n=7), Lambda light chain in 2% (n=4) and Biclonal in 4.5% (n=9).

Conclusion: Among patients referred to our clinical lab, monoclonal gammopathy was found in 3.98 percent of persons. IgG was the most frequently found Ig class (50.2%), followed by IgA (30.9%).Our findings can be the basis of future screening programs and preventive strategies.

Keywords: monoclonal gammopathy, isotype, prevalence

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Abbreviations: MGs, monoclonal gammopathies; MGUS, monoclonal gammopathy of undetermined significance; MM, multiple myeloma; CZE, capillary zone electrophoresis

Introduction

Monoclonal gammopathies (MGs) are B-cell lympho proliferative disorders caused by a clonal proliferation of B lymphocytes that produce a homogeneous immunoglobulin called M-protein.[1,2] Their clinical spectrum ranges from monoclonal gammopathy of undetermined significance (MGUS; a benign disorder characterized by monoclonal immunoglobulin level of <30g/L and a percentage of plasma cells in bone marrow of <10%) to the full-blown disease multiple myeloma (MM). Other B lympho proliferative disorder associated with M-proteins include: waldenstrom's macro globulinemia, plasmacytoma, non-hodgkin lymphoma, chronic lymphocytic leukemia, primary, and heavy and light chain amyloidosis diseases.[1,3] MGUS are much more common than MM and their incidence is age dependent. The prevalence of MGs is about 1% in individuals up to the age of 60 and about 10% in people older than 80 years of age.[4] The first screening study of M-protein was conducted in a southern Swedish district. M-proteins were found in 64 subjects above 25 years of age out of 6995. A clear increase with age was seen MGUS.[5] This study is the experience of our clinical laboratory with regard to the distribution of MGs and isotypes of M-component in samples collected for 2 years.

Patients and methods

From June 21, 2012 to June22, 2014, a total number of 18489 Iranian patients from the entire district were included in our study. All patients who referred to Noor Pathobiology Lab have a specific case number that prevents mistake with other patients. A 10-mL blood specimen was collected from all patients after they fasted overnight. Collected specimens from other laboratories were shipped on dry ice by express mail to our laboratory for further analysis. Serum was immediately separated and promptly frozen at -70°C. All serum samples were processed and analyzed in the same manner in Department of Electrophoresis and Coagulation of our lab. The samples were thawed and analyzed on average three days after blood collection. Serum protein electrophoresis was performed by Capillary Zone Electrophoresis (CZE) technique on a CAPILLARYS 2 instrument (Sebia, Issy-les-Moulineaux, France). CZE can be combined with immuno subtraction to determine the type of immuno globulins. Briefly, the sample is treated with individual anti-serum to remove the corresponding immunoglobulin by precipitating. The specific immuno type is demonstrated as a reduction of the peak on CZE.[6] Prevalence of monoclonal gammopathy, the distribution in different genders and ages, and the distribution of the heavy and light chain isotypes of M-protein was examined. Data were analyzed using Microsoft Excel 2013. Results are shown in simple proportions tables.

Results

Baseline Characteristics

A total of 18489 subjects participated in this study. Blood samples collection and serum protein electrophoresis were performed on all subjects. Baseline characteristics of study participants are shown in (Table 1).

Incidence of Monoclonal Gammopathy

A total of 736 patients were identified with monoclonal gammopathy That 197 Cases (82 women and 115 men) were immuno typed.

Age group distributions of immuno typed patients are shown in (Table 2).

Table 1 Frequency of subjects according to age group and sex

Sex/ Age	0-29	30-39	40-49	50-59	60-69	≥70	Total
Male	1367	985	1294	1558	1511	2054	8769
Female	1436	1273	1528	1988	1674	1820	9720
Total	2803	2258	2822	3546	3185	3874	18489

Table 2 Prevalence of monoclonal gammopathy according to age group and sex among the screened subjects

Age Group (years)	Male (%)	Female (%)	Total (%)
0-29	4 (0.29%)	4(0.28%)	8 (0.29%)
30-39	1 (0.1%)	11 (0.86%)	12 (0.53%)
40-49	49 (3.79%)	41 (2.68%)	90 (3.19%)
50-59	92 (5.9%)	78 (3.92%)	170 (4.79%)
60-69	134 (8.87%)	82 (4.9%)	216 (6.78%)
≥70	150 (7.3%)	90 (4.94%)	240 (6.2%)
Total	430 (4.9%)	306(3.15%)	736(3.98%)

Distribution of Isotypes Among Monoclonal Gammopathies

Information on the Ig isotype of the monoclonal protein was available for 197 cases. The most common isotype was IgG/Kappa (33.5%), followed by IgA/Kappa (23.3%), IgG/Lambda (16.7%), IgA/Lambda (7.6%), IgM/Kappa (7.6%), Biclonal (4.5%) and Kappa Light Chain (3.5%), Lambda Light Chain (2%), IgM/Lambda (1%), as shown in (Table 3).

Table 3 Distribution of M-protein isotype among patients with a monoclonal gammopathy

M-Protein Isotype	Frequency	Age (Average)	Male/ Female	Prevalence
IgG/Kappa	66	61.8	41/25	33.5%
IgG/Lambda	33	62.3	14/19	16.7%
IgA/Kappa	46	65.4	28/18	23.3%
IgA/Lambda	15	58.7	9/6	7.6%
IgM/Kappa	15	68.8	12/3	7.6%
IgM/Lambda	2	75.5	1/1	1%
Kappa Light Chain	7	63.2	4/3	3.5%
Lambda Light Chain	4	51.7	1/3	2%
Biclonal	9	67.1	5/4	4.5%

Discussion

The true frequency of MG can only be estimated by random sampling of a population. Studies of MG and isotype distribution have only been performed very rarely such as our study provides an estimate that gives the basis for comparison with other similar studies. The incidence rose with age and a male preponderance in the older groups became apparent. Supposedly, the increased incidence with age reflects increasing sensitivity in detection methods. Monoclonal gammopathy was found in 3.98 percent of population. IgG was the most frequently found Ig class (50.2%), followed by IgA (30.9%),which was consistent with results of a Ghanaian study (74%),[7] a Japanese study (73.6%),[8] an American study (68.9%),[9] and an Iceland study (55%).[10]

Consistent with previous studies,[8,11-13] we found that the rate of MG in men was approximately 1.5-fold of women (4.9% vs. 3.15%). however, several studies reported that prevalence of MG rose with age[5,8,9,14] and our Study also showed that prevalence of MG increased with age. we reported prevalence of MG across several age groups. For example, the prevalence of MG in those older than 70 years (6.2%) was approximately twice of those aged 40-49 years (3.19%) and 12-fold of those aged 30-39 years (0.53%). This finding is important as the Iranian society rapidly transforms from an aging society to an aged society. Our findings demonstrating the increased risk of MG with aging are useful in estimating medical costs for the elderly population. This is the first report of the prevalence of MG among Iranian Subjects.

The findings of this study raise questions that need further research. For example, although the data are convincing for the effect of age on prevalence of MG, but the underlying mechanisms are poorly understood. The increase in prevalence with age suggests that the occurrence of monoclonal gammopathies may reflect loss of control of limited response to antigenic stimulation with age and may involve age-related loss of immune surveillance. This is supported by the fact that immuno suppression related to drug therapy or disease also increases the risk of MG. An increased incidence of MG is documented in immuno compromised and immuno suppressed patients. For example, Patients infected by HIV virus have a substantially higher risk of MG than that of HIV-seronegative patients of the same age.[15,16] Also several studies show that MG occurs at a younger age of HIV infected patients than in the normal population.[17,18] Also, the incidence of MG in patients receiving immunosuppressive therapy is higher. For example, the incidence of MG is significantly greater in patients receiving kidney transplant.[19] Second, it is still unclear from a pathogenesis

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Conflicts of Interest

There is no conflict of interest.

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