Original Study

Prevalence of Monoclonal Gammopathy of Undetermined Significance in India—A Hospital-based Study

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Abstract

A cross-sectional hospital-based study was undertaken during a 3-month period to ascertain the prevalence of monoclonal gammopathy of undetermined significance (MGUS) in North India. Of the 3429 patients evaluated, MGUS was detected in 49 (1.43%) and multiple myeloma (MM) in 6 (0.17%). To the best of our knowledge, the present study is the first systematic study of the prevalence of MGUS in an Indian population. Our results highlight the relatively low incidence of MGUS in Indians compared with that in white and black populations. The incidental detection of MM in our study points to the need for creating awareness regarding myeloma-related symptoms in appropriate age groups.

Background: We sought to determine the prevalence of monoclonal gammopathy of undetermined significance (MGUS) in a hospital-based cohort in India. **Patients and Methods:** From March 2015 to May 2015, 3429 patients (age range, 40-88 years) were enrolled in the present study. Of the 3429 enrolled patients, 2354 (68.6%) were men and 1075 (31.4%) were women. Serum samples were collected from all patients and analyzed using serum protein electrophoresis (SPEP). The positive SPEP samples were subjected to immunofixation. The patients with positive results for both SPEP and immunofixation were registered in the oncology department and investigated further for plasma cell dyscrasias. **Results:** Of the 3429 study patients, 49 (1.43%) were found to have MGUS, and multiple myeloma was diagnosed in another 6 (0.17%). The prevalence rate of MGUS in patients aged 40 to 49, 50 to 59, 60 to 69, and 70 to 80 years was 0.83%, 1%, 2.62%, and 1.75%, respectively. Of the 49 MGUS patients, 5 (10.2%) were in the high-intermediate risk category using the Mayo Clinic criteria for risk stratification. At 30 months of follow-up, 1 patient in the high-intermediate category had developed multiple myeloma. **Conclusion:** To the best of our knowledge, the present study is the first systematic study on the prevalence of MGUS in an Indian population. The overall prevalence of MGUS was 1.43% in the evaluated Indian cohort, lower than that reported for white and black populations. The incidental detection of 6 subjects with multiple myeloma of 3429 screened subjects in our study was high compared with the reported incidence of multiple myeloma in India of only 1.9 per 100,000 persons. This finding indicates the need to create awareness about myeloma-related symptoms and screening studies in appropriate age groups, at least in the hospital-based setting.

Clinical Lymphoma, Myeloma & Leukemia, Vol. ■, No. ■, ■-■
Keywords: Cancer screening, Incidental myeloma, MGUS, M-protein, Prevalence in India

Introduction

Monoclonal gammopathy of undetermined significance (MGUS) is defined by the production of monoclonal protein without any systemic effects. Because MGUS is asymptomatic, the detection of MGUS is incidental during routine blood tests. The incidence of MGUS has been shown to increase with age and is influenced by

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Submitted: Jan 28, 2018; Revised: May 18, 2018; Accepted: Jun 4, 2018

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2152-2650/$ - see frontmatter
https://doi.org/10.1016/j.clml.2018.06.005

ethnicity, sex, a family history of a plasma cell proliferative disorder, and radiation and pesticide exposure.[1,2] Previous studies have reported a greater prevalence of MGUS in blacks and a lower prevalence rate in those of Asian descent compared with whites.[3-9] Because differences exist in the prevalence of MGUS among various ethnic groups, epidemiologic data from additional populations are required to assess the disease burden in Asia.

It has long been known that patients with MGUS have a greater risk of progression to multiple myeloma (MM) than those without MGUS.[10] A retrospective analysis of large patient cohorts has established MGUS as a precursor to MM.[11,12] Long-term follow-up studies have demonstrated that the overall risk of progression of MGUS to a plasma cell proliferative disorder is 1% annually.[10-13] Recent studies have demonstrated an increased risk of skeletal and renal events in patients with MGUS compared with those without MGUS.[14] In addition, overt MM is associated with significant morbidity and mortality; hence, it is imperative that the factors responsible for the transition from MGUS to overt myeloma are known to allow for the development of possible interventions in the future that could help prevent the progression to symptomatic disease.

The present study was undertaken to generate data on the prevalence of MGUS in Indian subjects and to develop a database for monitoring these patients for long periods to assess their risk of developing symptomatic disease.

Patients and Methods

A total of 3429 patients attending outpatient department (OPD) clinics at All India Institute of Medical Sciences for nonmalignant diseases were investigated in the present cross-sectional study during a 3-month period from March 2015 to May 2015. All sequential patients aged $\geq$ 40 years for whom blood chemistry investigations were performed at the hospital during the 3-month period were enrolled. All the participants provided written informed consent in accordance with the guidelines of the institute ethics committee. The serum remaining after completing the requisitioned biochemical investigations was used for the present study.

Serum protein electrophoresis (SPEP) was performed on all serum samples in accordance with the manufacturer's recommendations (Helena Biosciences Europe, Gateshead, UK). Immunofixation was performed on all the sera that tested positive for an M-band using SPEP. The patients with a confirmed M-band using SPEP and immunofixation were then counseled to undergo a complete evaluation for MM. The investigations included a complete blood count, blood chemistry (lactate dehydrogenase, β_2-microglobulin, IgG, IgA, IgM), 24-hour urine protein, liver and kidney function tests, a skeletal survey, and a bone marrow examination. A serum-free light chain assay was performed on samples testing positive for an M-band using Freelite (The Binding Site, Birmingham, UK). A serum-to-free light chain ratio $>$ 1.65 g/dL or $<$ 0.26 g/dL was considered an abnormal finding.

The diagnosis of MGUS was determined using the criteria defined by the International Myeloma Working Group: the presence of a monoclonal band at $<$ 3 g/dL, bone marrow plasmacytosis of $<$ 10%, the absence of end-organ damage (ie, no hypercalcemia, renal failure, anemia, bone lesions), and amyloidosis that can be attributed to the plasma cell proliferative disorder.[15] The study participants with a diagnosis of MM and/or another hematologic disorder were excluded from the present study. The prevalence rates were calculated by dividing the number of participants with MGUS in each age and sex category by the total number of participants in that category. The patients were considered to have low-, intermediate-, or high-risk MGUS using the Mayo Clinic criteria for risk assessment for MGUS.[16]

Results

The remaining sera samples were obtained from 3429 participants from March 2015 to May 2015. The baseline characteristics of the study participants are listed in Table 1. The median age was 54 years (range, 40-88 years), with 65% of the study population aged 40 to 59 years. The median age was 55 years (range, 40-88 years) for the men and 52 years (range, 40-85 years) for the women.

An M-band was detectable in 55 subjects (1.6%). Further investigations showed that 6 patients (0.17%) had MM. Of these 6 patients, 2 had stage I, 3 had stage II, and 1 had stage 3 using the International Staging System. The monoclonal bands were IgG-κ in

Table 1 Age and Sex Distribution of Participants Screened for MGUS (n = 3429)

Variable	Participants, n (%)
Gender	
Male	2354 (68.6)
Female	1075 (31.4)
Age, y	
40-49	1198 (35.0)
50-59	1031 (30.0)
60-69	0914 (26.7)
70-80	0286 (8.3)
Age group, y	
40-49	
Total with MGUS	10/1198 (0.83)
Men with MGUS	6/753 (0.80)
Women with MGUS	4/445 (0.90)
50-59	
Total with MGUS	10/1031 (1.0)
Men with MGUS	6/717 (0.84)
Women with MGUS	4/314 (1.27)
60-69	
Total with MGUS	24/914 (2.62)
Men with MGUS	19/664 (2.86)
Women with MGUS	5/250 (2.0)
70-80	
Total with MGUS	5/286 (1.75)
Men with MGUS	4/220 (1.80)
Women with MGUS	1/66 (1.52)
Total	
Total with MGUS	49/3429 (1.43)
Men with MGUS	35/2354 (1.44)
Women with MGUS	14/1075 (1.30)

Abbreviation: MGUS = monoclonal gammopathy of undetermined significance.