# **RESEARCH NOTE**

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# Paradigm shift in age of multiple myeloma patients: a study from a tertiary care government oncology hospital in Pakistan

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### **Abstract**

**Purpose** Multiple myeloma is a hematological disorder characterized by the presence of clonal plasma cells in the bone marrow that produce anemia, bone lesions, and kidney disease. The aim of this study was to determine the clinicopathological profile including age, sex, common symptoms and stage of patients with multiple myeloma diagnosed and managed in a government sector hospital in Pakistan.

**Patients and methods** This retrospective cross-sectional study was conducted over a period of eight years at the Institute of Nuclear Medicine, Oncology, and Radiotherapy in Islamabad. Of the 89 patients diagnosed and treated in this hospital, 81 patients with complete data were included in the study.

**Results** Of the 81 patients, 55 were males and 27 were female patients. The mean age at diagnosis in our set of patients was 53 years, with 79% of the patients aged  $\leq$  60 years of age. The most common presenting symptom was bone pain followed by generalized fatigue and infections. The most common monoclonal gammopathy was  $\log G_12.3\%$  patients were in stage I, 48.1% in stage II and 39.5% in stage III.

**Conclusions** Our study revealed that the patients in our institution presented multiple myeloma at much younger age than the patients seen in developed countries of the world. Most studies from Pakistan present data from private sector hospitals. This is the first study conducted at a Pakistani government hospital in patients with multiple myeloma. More studies should be conducted representing patients from both private and government hospitals to understand the true magnitude of the disease and the factors behind this age difference in patients with multiple myeloma in our part of the world.

**Keywords** Plasma cells, Multiple myeloma, Monoclonal immunoglobin, Renal insufficiency, Anemia, Diagnosis, Classification

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## Introduction

Plasma cell dyscrasias represent a group of heterogeneous diseases characterized by proliferation of monoclonal plasma cells. Plasma cell dyscrasias include MGUS (monoclonal gammopathy of undetermined significance), multiple myeloma, plasma cell leukemia, and plasmacytoma. Multiple myeloma is further subdivided into light chain myeloma, smoldering myeloma, non-secretory myeloma, IgD and IgE myeloma [1, 2]. In multiple myeloma, the proliferation of clonal plasma cells occurs in the bone marrow and monoclonal immunoglobin can be found in blood and urine. It can cause bone marrow failure and involves different systems of the body. Patients often present with anemia, lytic lesions, acute renal failure, and recurrent infections. Patients with multiple myeloma can be easily diagnosed even in resourceconstrained settings, with simple and easily available diagnostic modalities such as complete blood count, serum protein electrophoresis, bone survey, and bone marrow examination [3, 4].

Among the hematological malignancies, multiple myeloma is the second most common. It represents 1.8% of all cancer cases. Every year, it is diagnosed in 588,161 individuals worldwide [5, 6]. The incidence of myeloma is different in different parts of the world. It has continuously increased in the last 30 years, with a major increase in countries with a lower middle and lower sociodemographic index [7]. The global burden of multiple myeloma has increased by 126% and deaths by 94% between 1990 and 2016. There is an increased prevalence of multiple myeloma in Western Europe, North America, and East Asia [8]. According to our study the incidence of multiple myeloma has increased in Pakistan in the last few years. Epidemiological analyses are required to understand the incidence, prevalence, and management of cancer and is dependent on the presence of national cancer registries. In Pakistan, the development of cancer registries is in the preliminary phases. However, no single database exists that can provide a true overview of the tumor burden in all parts of the country [9-12]. A study evaluating the Lahore population showed cancer trends over a period of 30 years (1984–2014) [9] showed that among males, head and neck cancer, brain, lung cancer, and leukemia has increased while among females the incidence of ovarian, cervix, head and neck, and lymphomas has increased. This study did not mention any cases of myeloma [9]. Recently, a study conducted in Pakistan showed data on the incidence of myeloma cases recovered through three large hospitals located in Karachi, Lahore, and Islamabad. However, the three hospitals involved in the study were private sector hospitals [8].

This study was conducted in a government cancer hospital in the capital of Pakistan. It receives cases from all over the country specifically from northern areas. As it

is a government sector hospital, mainly patients of low socioeconomic status are admitted to this hospital. This study is unique in that is the first to report data from multiple myeloma patients from one of the largest government sector oncology hospitals in Pakistan.

### **Materials and methods**

This retrospective study was conducted at Nuclear Medicine, Oncology and Radiotherapy Institute (NORI). The study protocol was approved by the Ethics Committee and Institutional Review Board of NORI (IRB No.5 [13] / 101).

This is a government hospital located in the federal area of Pakistan. Although it is a government organization, it is equipped with state-of-the-art equipment. It is one of the few government organizations in Pakistan equipped with all the facilities for the diagnosis and treatment of cancer patients. Being a government organization, all facilities are available at very low rates and in some cases free of cost. One limitation of the study is that NORI mainly receives patients from the northern areas of Pakistan and most patients who come to this hospital have a low socioeconomic status. The study was conducted after receiving approval from the Ethics Review Board of the Hospital. Informed consent was taken from all the participants before commencements of study. We retrospectively compared data including age, gender, immunoglobulin class, symptoms and stage of the disease from newly diagnosed patients with myeloma from January 2015 to January 2023. Patients were diagnosed according to the International Myeloma Working Group (IMWG) criteria 2003 and its updated version [13]. All patients were classified at the presentation using the International staging system for Multiple Myeloma (ISS scoring system). All data were entered and analyzed usings SPSS v.23.

#### Results

The total number of patients diagnosed with multiple myeloma at our institute was 89. Eight patients had incomplete records and were excluded from the study. Of the 81 patients enrolled in the study, 55 were male patients and 27 were females. The patients were divided into 5 groups according to their age at the time of presentation. The age range of patients was 49 with a minimum age of 31 and maximum age of 80 with a standard deviation of 9.425.

The distribution of patients in different age ranges is shown in Fig. 1.

The main symptoms reported by the patients in decreasing order of frequency were bone pain (79%), generalized fatigue (15%), and infections (6%). Cytogenetic analysis was not performed for any of the patients. Patients were classified according to the ISS.

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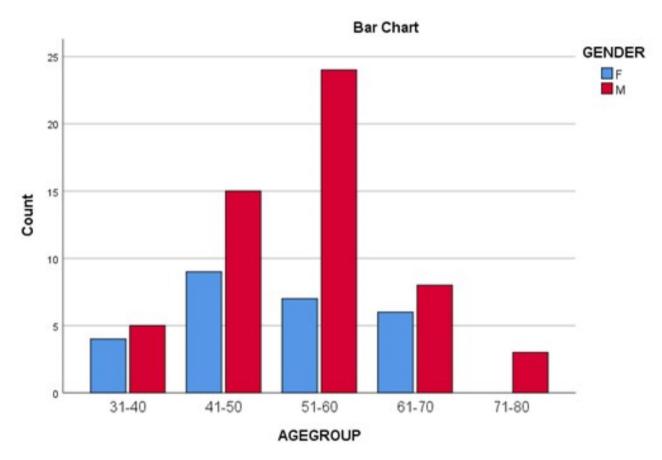


Fig. 1 Sex distribution of patients diagnosed with multiple myeloma in different age groups

The percentage of patients in different stages in relation to their age group is shown in Fig. 2: The most common monoclonal gammopathy was IgG in 92% of patients followed by IgA in the remaining patients (Fig. 2).

**Figure 3** Line graph showing gradual increase in incidence of multiple myeloma cases.

#### Discussion

Multiple myeloma is a plasma cell disease and is the second most common hematological neoplasm in developed countries. Multiple myeloma has a varied presentation spectrum. It is a disease associated with hypogammaglobinemia, bone marrow, and kidney involvement. Patients present with infection, severe anemia, and other symptoms of bone marrow failure. Studies conducted around the world show that the incidence of myeloma is highest in North America, Europe, and Asia, but mortality is highest in Asia. There also appears to be a difference between the number of cases in the developed world and low-middle-income countries. One of the reasons for the higher mortality is the lack of diagnostic facilities and the expense of available treatments [3, 14, 15].

In our study, we reported 89 patients with newly diagnosed multiple myeloma over a period of seven years.

The male to female ratio in our study was 2:1, which is comparable to a study by Basit et al. from the Shaukat Khanum Hospital in Lahore [16]. The mean age at diagnosis in our cohort of patients was 53 years, with 79% of patients ≤ 60 years of age. This contrasts with the study done by Turesson et al. from Sweden [17]. Their study revealed a mean age of 70-74 years at the time of diagnosis. Similarly, another report in the US database showed that the mean age of patients with myeloma was 69 years at the time of diagnosis [6]. However, studies conducted in developing countries of the world revealed a lower age range at the time of diagnosis. Zaheer et al. conducted a study at the Armed Forces Institute of Pathology in Pakistan on 53 patients with multiple myeloma. The mean age of the patients was 59.9 years [18]. An analysis of different races and ethnic groups was conducted in the United States. They reported that the median age at diagnosis was 68 years among whites, 61 among blacks, and 66 years among Asians [19].

An international study conducted in 72 patients with myeloma showed 16% of the patients were diagnosed in stage 1, 9% of the patients in stage II, and 71% of the patients in stage III at the time of presentation [20]. Our study showed that 12% of our patients were in stage I, 48% were in stage II, and 39% were in stage III at the

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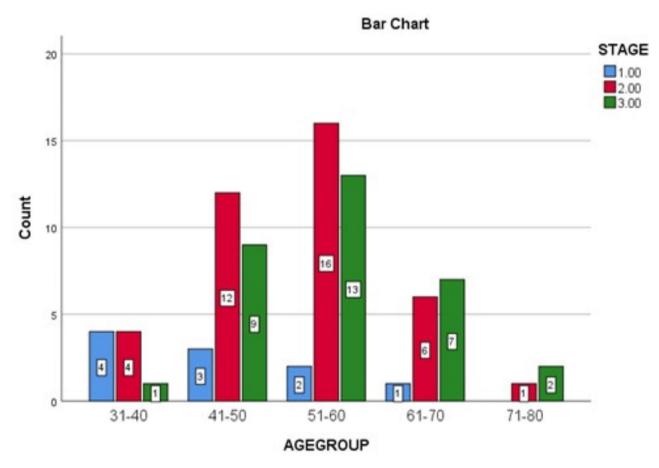


Fig. 2 Stage of patients with multiple myeloma at the time of presentation in different age groups

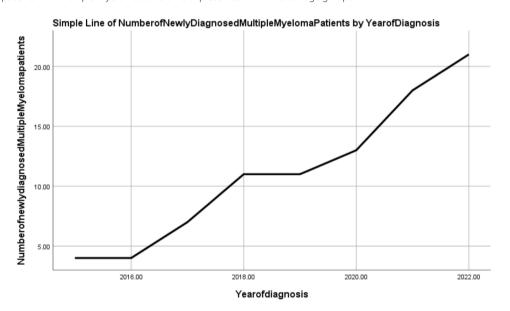


Fig. 3 shows an increase in cases of multiple myeloma over the period of time

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time of presentation. A study conducted in private sector hospitals of Pakistan showed that 27% patients were diagnosed in stage 1, 34% were patients in stage II, and 39% patients were in stage III [8]. When comparing our results with international data, most of these patients were in stage III. One reason for this difference could be the marked difference in the age of the patients at the time of presentation. Our study presents data from patients belonging to the lower socioeconomic class and most patients were in stage II at the time of diagnosis.

# **Conclusions**

We present data from one of the largest government sector cancer hospitals in Pakistan. To our knowledge, this was the first study on multiple myeloma in Pakistan that presents data on patients diagnosed and treated in a government sector hospital.

There has been an increase in patients with multiple myeloma with differences in the age of diagnosis, in our setting, as a greater proportion of younger patients present with the disease. The exact cause of lower age incidence is unknown however because younger population is more likely to pursue and obtain medical care than older age population in resource constrained developing country like Pakistan, this might be responsible for lower age incidence of multiple myeloma in our country. Another possible explanation could be that inhabitants of developing and lower middle-income countries are younger and thus can result in unequal and over representation.

This study provides important information for the establishment of national registries that encompasses data encompassing all private and government hospitals in Pakistan to better understand the true burden of the disease and the etiological factors causing its presentation in younger age groups.

#### Abbreviations

NORI Nuclear Medicine Oncology & Radiotherapy Institute
MGUS Monoclonal gammopathy of undetermined significance

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None.

#### Author contributions

First author wrote the main manuscript, second author helped in writing the manuscript and research process. Third author participitated in analysing the data and preparing figues. All the authors reviewed the manuscript.

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We have no funding sources to declare.

#### Data availability

This research contains data of patients, it cannot be shared openely, however it is available on reasonable request.

#### **Declarations**

#### Human ethics and consent to participate

The study protocol, human ethics and consent to participate was approved by the Ethics Committee and Institutional Review Board of NORI (IRB No.5 [13] /101)

#### Consent for publication

Consent for publication has been obtained.

#### **Competing interests**

The authors declare no competing interests.

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