RESEARCH ARTICLE

Adult Primary Myelodysplastic Syndrome: Experience from a Tertiary Care Center in Pakistan

Sadia Sultan[1]*, Syed Mohammed Irfan[2]

Abstract

Background: Primary myelodysplastic syndrome (MDS) is an acquired clonal disorder of myeloid progenitor cells, characterized by peripheral cytopenias in the presence of hypercellular marrow with dysplastic features. Our aim was to study the demographical and clinicopathological features of adult Pakistani patients with MDS at disease presentation. Materials and Methods: This single centre study was conducted at Liaquat National Hospital and Medical College, extending from January 2010 to December 2014. Data were retrieved from the patient archives. Results: Overall 45 patients were diagnosed at our institution with de novo MDS during the study period. There were 28 males and 17 females. Age ranged between 18 and 95 years with a mean age of 57.6±17.4 years and median of 64 years. The male to female ratio was 1.7:1. The main presenting complaints were generalized fatigue (60%), fever (33.3%), dyspnea (15.5%), bleeding (13.3%) and weight loss (11.1%). Examination was unremarkable in 42.2% of patients. Physical examination revealed pallor in 37.7%, followed by petechial and purpuric rashes in 20%. The commonest laboratory finding was anemia (hemoglobin < 10 g/dl in 41 (91.1%) patients. Out of these, 27 (60%) patients had normocytic anemia, followed by macrocytic (22.2%) and microcytic (8.8%). Conclusions: Primary MDS in Pakistani patients demonstrates a male preponderance. The proportion of anemic patients was high in our series with predominance of normocytic anemia. However, other clinico-hematological features appear comparable to published data.

Keywords: Primary -myelodysplastic syndrome - adults - Pakistan

Asian Pac J Cancer Prev, **17 (3)**, 1535-1537

Introduction

Myelodysplastic syndrome (MDS) are a group of clonal disorders characterized by ineffective hematopoiesis, cytopenias, in the presence of hypercellular bone marrow with morphological dysplastic changes (Newman et al., 2012; Akinci et al., 2014). Myelodysplasia is a heterogeneous disease with an increased risk of leukemic transformation, overall 40% of patients will transform to AML during the disease course (Chevassut et al., 2011; Gao et al., 2015).

The estimated incidence of MDS is 3-5 per 100,000 populations annually that increases to 20 to 50 cases per 100000 persons per year after 60 years of age (Bernasconi et al., 2005; Malcovati et al., 2013; Rashid et al., 2014). It occurs most commonly in the sixth to seventh decade of life, with the median age of ~70, but MDS has also been reported in pediatric population (Rodrigues et al., 2007; Neukirchen et al., 2011).

MDS pathophysiology is multifactorial, involving chromosomal changes or genetic mutations and widespread gene hypermethylation at advanced disease stages (Fenaux et al., 2014). The disease can be broadly segregated into primary and secondary entities, depending on whether its de novo MDS or arises as a result of preceding exposure to chemotherapy, ionizing radiation and various chemicals (Schnatter et al., 2008).

The diagnosis of MDS is mainly reliant on evaluation of the bone marrow dysplasia associated with unexplained peripheral cytopenias in an appropriate clinical background. Ineffective hematopoiesis leads to symptomatic peripheral cytopenias. Patients with MDS usually develop severe anemia and require frequent blood transfusions. These patients are also prone to develop recurrent infections, fever, fatigue, easy bruising and bleeding complications secondly to cytopenia. The outlook in MDS depends on the type and its severity.

Most published data on MDS is from Western countries. Published local data are scarce. There are few studies are available from Pakistan (Irfan et al., 1998; Ehsan et al., 2010; Rashid et al., 2014). The purpose of this study is to demonstrate demographical, clinical and the hematological features of adults primary MDS patients who visited our tertiary care center from 2010 till the end of 2014.

*[1]Department of Hematology and Blood Bank, Liaquat National Hospital and Medical College, [2]Liaquat National Medical College, Karachi, Pakistan *For correspondence: sadiasultan96@yahoo.com*

Materials and Methods

This retrospective analysis was carried out at the Department of Haematology, Liaquat National Hospital, Karachi, from January 2010 to December 2014. All the patients diagnosed during the study period were included in the study by non-probability purposive sampling.

Patients having history of preceding hematological disorders like Chronic myeloid leukemia, Myeloproliferative neoplasm and with prior history of chemotherapy were excluded from the study. The patients who were known cases of secondary MDS were also not included. Based on this, 45 patients who fulfilled the WHO criteria for primary MDS were enrolled in the study. The diagnosis of MDS was ascertained according to the standard WHO criteria, and was based on peripheral cytopenias, bone marrow dysplasia and percentage of blast cell counts (Brunning et al., 2008).

The blood samples from the patients were tested by Automated Cell Dyne counter for complete blood counts including hemoglobin, total leucocyte count and platelet count and mean cell volume. Bone marrow samples were taken from posterior iliac crest through Jamshidi needle and were stained by Leishman's stain. Perl's stain was carried out on each bone marrow smears by commercially provided kits from Merck Diagnostic according to manufacturer's instructions.

Approval from the institutional ethical and research review committee was obtained prior to the study.

Statistical analysis

Statistical Package for the Social Sciences version 22.0 (SPSS Inc, Chicago, IL, USA) was used for statistical analysis. Descriptive variables was presented as mean (SD). Data was presented as frequencies and percentages.

Results

Out of total 45 patients, 28 were males (62.2%) and 17 were females (37.7%) with male to female ratio of 1.7:1. The mean age of patients at presentation was 57.6±17.4 (range 18-95) years with the median age of 64 years. Age stratification is shown in table-1.

The main presenting complaints were generalized fatigability in 27 (60%) patients, fever in 15 (33.3%) patients, and dyspnea in 7 (15.5%) patients, bleeding in 6 (13.3%) patients and weight loss in 5 (11.1%) patients. Examination was unremarkable in majority (42.2%) of patients. Physical examination revealed pallor in 17 (37.7%) patients, followed by petechial and purpuric rashes in 9 (20%) patients.

The mean hemoglobin was 7.7±2.4g/dl (3.6-12.5) with the mean MCV of 98.4±18.9 fl. The mean total leukocyte count of 5.7±5.8x10^9/l (0.6-18.8); mean Absolute neutrophilic count (ANC) of 3.0±5.4x10^9/l and the mean platelets count were 82.7±104.6x10^9/l (5-244).

The commonest laboratory findings was anemia; Hemoglobin <10 g/dl in 41 (91.1%) patients. Out of which 27 (60%) patients had normocytic anemia, followed by macrocytic (22.2%) and microcytic (8.8%) anemia's respectively. Thrombocytopenia (platelets count <100x10^9/l) was detected in 34 (75.5%) patients, while severe thrombocytopenia (platelets <20x10^9/l) was seen in 9 (20%) patients. While neutropenia (ANC<1.8x10^9/l) was noted in 20 (44.4%) patients. Pancytopenia and bicytopenia was noted in 18 (40%) and 14 (31.1%) patients respectively.

Table 1. Age Stratification in Adult Patients with Primary Myelodyspastic Syndrome

Age groups	Male n=28	Female n=17	Total n=45	Percentage %
18-30	3	1	4	8.8
31-50	6	4	10	22.2
51-65	7	5	12	26.6
66-95	12	7	19	42.2

Discussion

Myelodysplastic syndrome comprises a very heterogeneous group of myeloid neoplasms, originating from hemopoeitic stem cell. This hematological disorder is not uncommon in Pakistan, but due to insufficient diagnostic facilities and virtual lack of health education they often remain undiagnosed.

Limited studies are available from Pakistan on MDS.

We have described a series of 45 MDS cases followed at our institution including their demographical, clinical and hematological profiles.

It is persistently established that MDS is the disease of elderly age with the median age of approximately 65–70 years. Previously two studies conducted in Pakistan have reported a median age of 60 and 59 years, which is in parallel with our findings (Rashid et al., 2014; Irfan et al., 1998). Analogous to this, a large regional study reported from China has shown the median age of 58 years (Wang et al., 2008). Another study from Singapore had reported a mean age of 64 years (Lau et al., 2004). Similar to us, a regional study reported by Shah et al from neighboring India, revealed the mean age of MDS patients as 55 years at disease presentation (Shah et al., 2009).

When compared with earlier international reports, our results are in conflict with studies published from Europe and France, where the mean age for MDS is above 70 years (Iglesias et al., 2003; de Hollanda et al., 2011). Conceivably, this difference may be clarified by obvious variation between two racial groups based on genetic composition and also the higher average age in western countries.

In this study, which consisted of 45 patients with primary MDS, the male to female ratio is 1.7:1 which is consistent with the well known male preponderance which has been reported from other regional and international studies (Akinci et al., 2014; Rashid et al., 2014).

In general, these patients are prone to have repeated infections, anemia, easy fatigue and bleeding manifestations secondary to peripheral cytopenias. The clinical manifestations of MDS are heterogeneous and patients are usually symptomatic. Among our patients majority presented with generalized weakness and easy fatigability. Similar presenting symptoms were observed

by prior Indian (63.3%) and Pakistani (80%) studies conducted by Shah and Ehsan et al respectively (Shah et al., 2009; Ehsan et al., 2010). Clinical features in our study somewhat correlated with the study conducted by Lau et al from Singapore showing that symptomatic anemia and bleeding was seen in 60.5% and 14% respectively (Lau et al., 2004).

Anemia is the frequent manifestation in MDS and was seen as a common finding (91.1%) in our patients. Comparable findings have been reported in other studies on MDS. When compared with earlier reports, our results are in concurrence with studies which reported 93.4% and 84.5% prevalence of anemia in the regional studies (Ehsan et al., 2010; Rashid et al., 2010). We determined normocytic anemia as a predominant type of anemia in our series.

This disorder is characterized by one or more cytopenias despite a relatively hypercellular bone marrow. The presence of pancytopenia and/or thrombocytopenia at the time of diagnosis in MDS patients has been described as poor prognostic markers (Akinci et al., 2014). In the present study pancytopenia and bicytopenia were noted in 40% and 31.1% respectively, more or less similar to earlier studies reported from Pakistan (71.7% and 26%) and turkey (55% and 40%) (Ehsan et al., 2010; Akinci et al., 2014).

Lastly limitations of our study need to be mentioned. The sample size in our study is relatively small. A larger sample size study would be a better indicator of demographical, clinical and laboratory attributes in our patients population. Secondly the follow-up data for disease outcome is not available.

In conclusion, the study strengthen that MDS in Pakistani patients is seen in comparatively young age and mostly patients have symptomatic anemia and easy fatigability as a presenting feature. Other presenting features are similar as reported in literature. Prospective studies should be pursueded on a large number of patients to explicate further disease spectrum, demographic and obviously should incorporate prognostic karyotyping and molecular testing in Pakistani population.

References

Akinci S, Silay K, Ulas A, et al (2014). Neutrophil to lymphocyte ratio--not an independent prognostic factor in patients with the myelodysplastic syndrome. *Asian Pac J Cancer Prev*, **15**, 10883-5.

Bernasconi P, Klersy C, Boni M, et al (2005). Incidence and prognostic significance of karyotype abnormalities in de novo primary myelodysplastic syndromes: a study on 331 patients from a single institution. *Leukemia*, **19**, 1424-31.

Brunning RD, Orazi A, Germing U, Le Beau MM. Myelodysplastic syndromes/neoplasms, overview. In: Swerdlow HS, Campo E, Haris LN, et al (2008). WHO classification of tumours of haemopoietic and lymphoid tissues. Lyon: International agency for research on cancer, **89**.

Chevassut TJ, Mufti GJ (2011). The myelodysplastic syndromes. In:Hoffbrand AV, Catovsky D, Tuddenham EG, Green AR. Post graduate hematology, 6th edition, **503**.

de Hollanda A, Beucher A, Henrion D, et al (2011). Systemic and immune manifestations in myelodysplasia: a multicenter retrospective study. *Arthritis Care Res (Hoboken)*, **63**, 1188-94.

Ehsan A, Aziz M (2010). Clinico-haematological characteristics in Pakistani patients of primary myelodysplastic syndrome according to World Health Organization classification. *J Coll Physicians Surg Pak*, **20**, 232-6.

Fenaux P, Haase D, Sanz GF, et al (2014). ESMO guidelines working group. Myelodysplastic syndromes: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol*, **25**, 57-69.

Gao S, Li Z, Fu JH, et al (2015). Decitabine in the treatment of acute myeloid leukemia and myelodysplastic syndromes, which combined with complex karyotype respectively. *Asian Pac J Cancer Prev*, **16**, 6627-32.

Irfan M, Kakepoto GN, Khursheed M (1998).Primary myelodysplastic syndrome: clinical spectrum of 53 cases. *J Pak Med Assoc*, **48**, 69-73.

Iglesias Gallego M, Sastre Moral JL, Gayoso Diz P, et al (2003). Incidence andcharacteristics of myelodysplastic syndromes in Ourense (Spain) between 1994-1998. *Haematologica*, **88**, 1197-9.

Lau LG, Chng WJ, Liu TC, et al (2004). Clinico-pathological analysis of myelodysplastic syndrome according to French-American-British classification and international prognostic scoring system. *Ann Acad Med (Singapore)*, **33**, 589-95.

Malcovati L, Hellström-Lindberg E, Bowen D, et al (2013). Diagnosis and treatment of primary myelodysplastic syndromes in adults: recommendations from the European LeukemiaNet. *Blood*, **122**, 2943-64.

Newman K, Maness-Harris L, El-Hemaidi I, Akhtari M (2012). Revisiting use of growth factors in myelodysplastic syndromes. *Asian Pac J Cancer Prev*, **13**, 1081-91.

Neukirchen J, Schoonen WM, Strupp C, et al (2011). Incidence and prevalence of myelodysplastic syndromes: data from the Dusseldorf MDS-registry. *Leuk Res*, **35**, 1591-6.

Rodrigues EF, de Souza DC, Camargo A, et al (2007). Cytogenetic biclonality in a child with hypocellular primary myelodysplastic syndrome. *Cancer Genet Cytogenet*, **178**, 70-2.

Rashid A, Khurshid M, Shaikh U, Adil S (2014). Chromosomal abnormalities in primary myelodysplastic syndrome. *J Coll Physicians Surg Pak*, **24**, 632-5.

Shah NM, Prajapati SG, Adesara RP, Patel AP (2009). An analysis of 30 cases of myelodysplastic syndrome. *Indian J Pathol Microbiol*, **52**, 206-9.

Schnatter AR, Glass DC, Tang G, Irons RD, Rushton L (2008). Myelodysplastic syndrome and benzene exposure among petroleum workers: an international pooled analysis. *J Natl Cancer Inst*, **104**, 1724-37.

Wang XQ (2008). Sino-US shanghai leukemia cooperative group.who classification and cytogenetic analysis of 435 cases with myelodysplastic syndrome. *Zhonghua Nei Ke Za Zhi*, **47**, 464-7.