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A Single Centre Experience of Clinically Suspected Myelodysplastic Syndrome Cohort

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Author's contribution

This work was carried out in collaboration between both authors. Both the authors designed, analyzed, interpreted and prepared the manuscript.

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ABSTRACT

Purpose: 1. To study clinical, histo-morphological and cytogenetic profile of clinically suspected MDS cases. 2. Categorisation according to recent WHO classification, IPSS-R scoring and clinical outcome.

Methods: This was a retrospective study conducted over a period of 2 years from Jan 2019 to Dec 2020. Laboratory received blood, bone marrow aspirate and biopsy samples with clinical diagnosis of MDS was reviewed in correlation with outsourced cytogenetic study reports in Haematology laboratory services department, Apollo Hospitals Bannerghatta road, Bengaluru.

Results: Based on WHO criteria, out of 50 cases, eight cases belonged to category ICOUS, and 7 cases fell into others. Out of the 35 cases, MDS EB-2 was noted in 23% of the cases. 25 cases were sent for cytogenetic study and 7 were positive. One case was positive for Monosomy 7, 2 for Trisomy 8, 4 for 5q deletion, and one of it had 5q deletion with trisomy 8. Packed red blood cells (PRBC) was transfused in 11 patients. Decitabine was the commonest hypomethylating agent given in 10 patients followed by lenalidomide in 5 patients. Out of 11 MDS EB-1 and MDS EB-2 cases, four patient died and both categories showed statistically significant risk of association between disease and poor outcome.

Conclusion: MDS EB-1 and EB-2 was the second commonest WHO category collaterally having the highest IPSS-R score and worst prognosis. 5q deletion was the commonest cytogenetic abnormality seen.

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1. INTRODUCTION

Myelodysplastic syndrome (MDS) is a clonal disorder of hematopoietic stem cells. It is characterised by trilineage dyspoiesis and ineffective hemopoiesis. Clinical variability of MDS with histopathological and cytogenetic heterogeneity makes the diagnosis challenging. In about one third of the cases there is leukemic transformation [1]. Patients are commonly presented with signs of hematopoietic insufficiency, particularly symptoms of anemia; less often, susceptibility to infection and signs of bleeding [2].

Clinical features of MDS are nonspecific and imbricate with other haematological disorders like acute myeloid leukaemia (AML), myeloproliferative neoplasm, paroxysmal nocturnal haemoglobinuria, and aplastic anaemia [3]. The incidence of MDS increases with age. Patients with past history of chemotherapy and radiotherapy have around 10% greater risk of developing disease [2]. The diagnosis of MDS is based on the World Health Organisation (WHO criteria), and prognostication is done by revised international prognostic scoring system (IPSS-R) [4]. But in some cases of refractory cytopenia with minimal dyspoiesis, transfusion dependant macrocytic anaemia the dilemma of diagnosis still persists.

Diagnosis of MDS is based on morphological assessment that is examining peripheral smear and bone marrow examination, it can be subjective particularly in patients with early low risk disease. It is calculated that diagnostic discrepancy can occur at the time of initial presentation in close to 20% of patients. This can lead to implications for therapeutic decision making and patient counselling. Diagnosis is obvious in patients with excess blasts [5].

Risk adapted therapy is the current strategy for the treatment of MDS. Options for newly diagnosed patients with lower risk of MDS include transfusion followed by erythroid and thrombopoietin growth factors. Low doses of hypomethylating agents are also proposed for poor prognosis lower risk MDS cases. Lenalidomide is approved for patients with lower risk MDS, anaemia and del5q patients [5].

1.1 Objectives

1. to study clinical, histo-morphological and cytogenetic profile of clinically suspected MDS cases. 2. Categorisation of our cases according to the recent WHO classification. 3. Final diagnosis with outcome of these cases will be analysed. 4. To score according to the R-IPSS scoring and impact on patient clinical outcome.

2. MATERIALS AND METHODS

This retrospective study was conducted at Apollo hospitals, Bannerghatta road, Bengaluru, Karnataka from Jan 2019 to December 2020.

Base line investigations included were complete hemogram, VitB12, folate, serum Iron studies. Bone marrow aspiration and biopsy were performed, stained with Leishman and Perls stain. Cytogenetic analysis was performed as outsourced test.

2.1 Inclusion Criteria

All cases with unexplained cytopenia.

2.2 Classification and Prognosis

Revised WHO criteria 2017 and revised IPSS-R guidelines [4] were followed.

2.3 Statistical Analysis

Statistical analysis was done by tabulating in the excel sheet. Fischer test was used to assess significance of association.

3. RESULTS

A total of 50 consecutive patients with clinically suspected myelodysplastic syndrome were included in this study, 35 patients were males, with age range from 10yrs to 85 years and highest number of cases in 61-70 years of age (Fig. 1). The most common presenting clinical symptom were weakness, fatigability and the most common laboratory findings were anaemia, and thrombocytopenia. Pancytopenia was noted in five cases.

In our study according to the WHO criteria, out of 50 cases 8 cases belonged to category of idiopathic cytopenia of undetermined significance (ICOUS), and 7 cases fell into others category (diagnosed as paroxysmal nocturnal hemoglobinuria, pure red cell aplasia, lymphoma). Out of the 35 cases MDS EB-2 was noted in 23% of the cases (Fig. 2). Out of the 35 cases, 25 were sent for cytogenetic study (other

10 cases refused due to financial constraints) and out of which, 7 were positive. One case was positive for Monosomy 7, 2 for Trisomy 8, 4 for 5q deletion, and one case had 5q deletion with trisomy 8 (Fig. 3).

Bone marrow aspiration revealed 4 patients with less than 5% blasts, 3 patients with MDS EB-1 showed blasts cells ranging from 5 to 9% and 8 patients of MDS EB-2 showed blasts cell ranging from 11 to 15%. Rest of cases had no blasts in bone marrow. Dyserythropoiesis (Fig. 4a) was the most common finding in about 21 cases followed by dysmegakaryopoiesis (Fig. 4b) and dysgranulopoiesis.

3.1 IPSS-R Score

All the 8 cases of MDS EB-2 had high IPSS-R score and one of the 4 cases with 5q deletion had high IPSS-R score, since it had 21% blasts (Table 1).

3.2 Treatment

Packed red blood cells (PRBC) was transfused in 11 patients. Among them 3 patients were given single unit of PRBC, 6 patients received 3 units and 2 patients received 4 units of PRBC transfusion in their course of admission. Decitabine was the commonest hypomethylating agent given in 10 patients followed by lenalidomide in 5 patients. Twenty-one out of the 50 cases were lost to follow up (Table 2).

3.3 Outcome and Prognosis

3 out of the 8 cases of MDS EB-2 and one of the MDS EB-1 died within 6 months to one year of follow up.

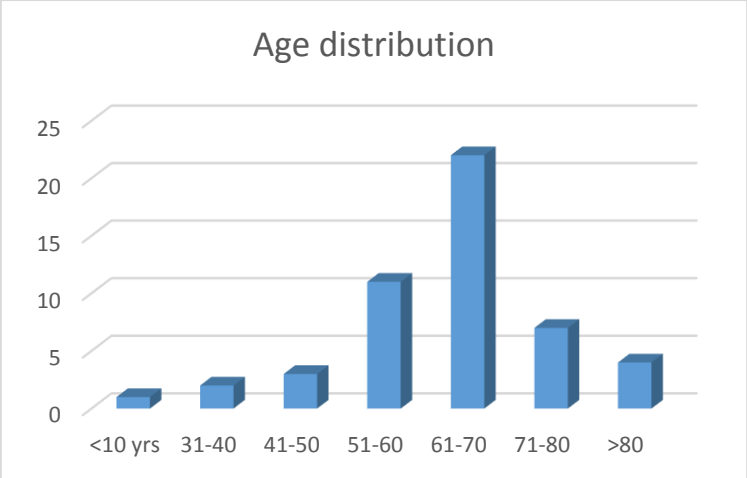

Fig. 1. Age distribution

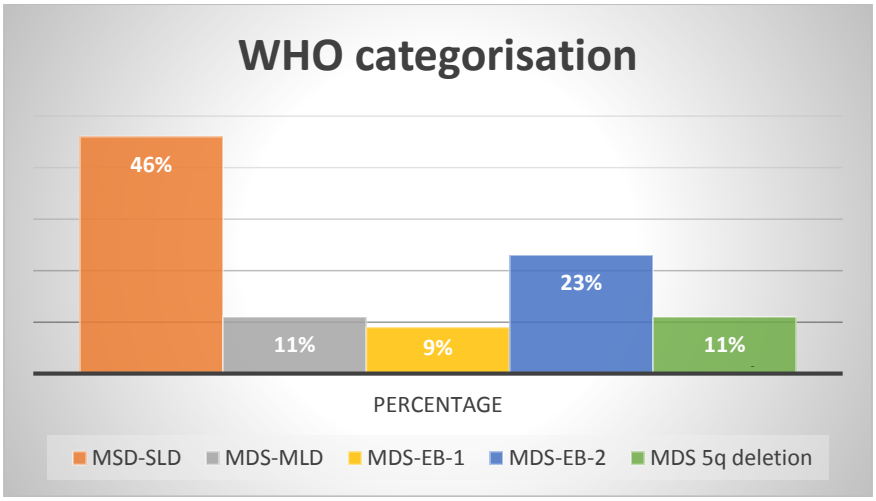

Fig. 2. Distribution of cases according to WHO classification

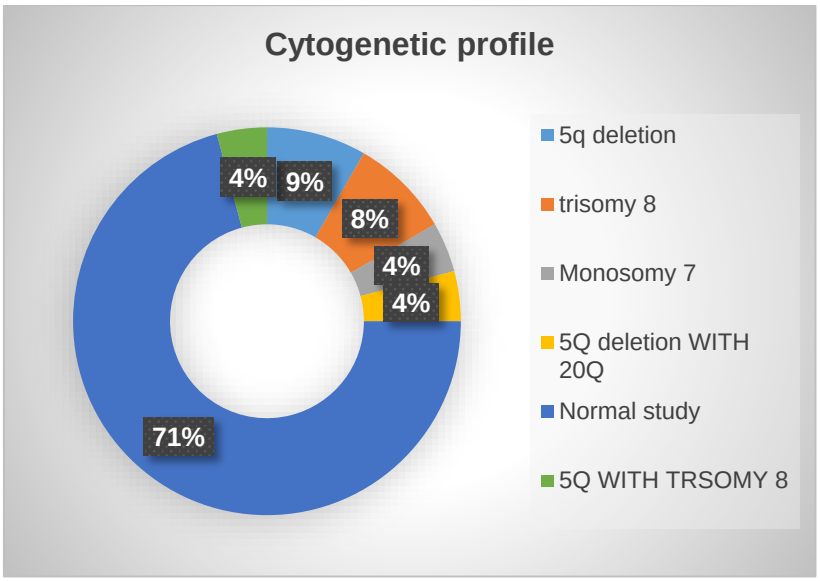

Fig. 3. Cytogenetic profile of 25 cases

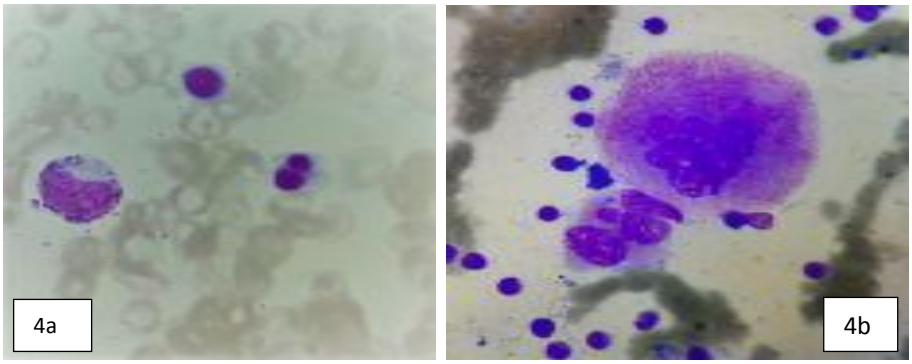

Fig. 4. Bone marrow aspirate showing binucleated erythroblast [4a] and dysplastic megakaryocyte [4b] Leishman's stain ×1000

Table 1. Categorisation of cases based on WHO classification and IPSS-R scoring

WHO categorisation	IPSS-R grade	IPSS-R score	Number of patients
MSD-SLD	Very low	</=1.5	7
	Low	>1.5-3	8
	Intermediate	>3-4.5	
	High	>4.5-6	1
	Very high	>6	
MDS-MLD	Very low	</=1.5	0
	Low	>1.5-3	3
	Intermediate	>3-4.5	
	High	>4.5-6	1
	Very high	>6	
MDS-EB-1	Very low	</=1.5	
	Low	>1.5-3	1
	Intermediate	>3-4.5	2
	High	>4.5-6	
	Very high	>6	
MDS-EB-2	Very low	</=1.5	
	Low	>1.5-3	

WHO categorisation	IPSS-R grade	IPSS-R score	Number of patients
	Intermediate	>3-4.5	3
	High	>4.5-6	5
	Very high	>6	
MDS 5q deletion	Very low	</=1.5	
	Low	>1.5-3	2
	Intermediate	>3-4.5	1
	High	>4.5-6	1
	Very high	>6	

Table 2. Multidisciplinary treatment given to MDS patients in our study

Treatment	ICOUS	MSD-SLD	MDS-MLD	MDS-EB-1	MDS-EB-2	MDS 5q deletion
Packed red blood cells	5	2	1	1	1	1
Erythropoietin	1		1	1		1
Thrombopoietin			1	1	1	
Decatibine		1	2	3	3	1
Lenalidomide		1			2	2
Single Donor Platelets				1		1
Vit B12	2					
No follow	12	4	1	1	2	1
Improved	4	1	3	1	2	2
Non improved	1			1		1
Death	1			1	3	1

4. DISCUSSION

The MDS is said to be a hematopoietic stem cell disease and many new concepts have evolved in the recent years though not complete. The WHO classification and IPSS-R are the most commonly used classification and scoring system to determine the course and prognosis of MDS cases.

The risk of MDS increases with advancing age; approximately 86% of patients with newly diagnosed MDS are 60 years old (median age, 76 years). In general, MDS is divided into 2 broad categories: primary (de novo) and secondary. Secondary MDS can be therapy related and is diagnosed after exposure to radiotherapy or cytotoxic chemotherapy [3].

Out of the total 50 cases in our study the male to female ratio is 2.3 which is in concordance with Kar et al. [6] and Narayanan [1]. Median age was 62 in concordant with Narayanan [1] and Ramesh Kumar et al. [7]. There was no significant association (P value is 0.485) between age and outcome in our study concordant with other studies.

The common symptoms presented in our study were weakness, tiredness, similarly reported by Shah et al. [8] and few also had bleeding tendency and occasional patients had bone pain especially in patients with MDS EB-2. Fever was not a common presentation though few of the patients had leukopenia and pancytopenia.

In our study the most common haematological abnormality was anaemia in 62%, followed by thrombocytopenia and pancytopenia in about 20% of the cases.

Regarding the findings in peripheral blood smear, we observed that normocytic normochromic anaemia was the most common morphology followed by macrocytic anaemia with mild dysgranulopoiesis. Thrombocytopenia was also evident in few cases. Blast percentage varied from 1% to 12%. Increase in blast percentage had direct and significant association to outcome (P value < 0.05). Hence, blast percentage is the most important predictive marker for outcome (death) and possible progression to AML as mentioned previous studies [4,9].

Bone marrow cellularity ranged from hypocellular to hypercellular. Dyserythropoiesis was the most common finding followed by dysgranulopoiesis and dysmegakaryopoiesis with blast percentage ranging from 1 to 12%.

The most common type of MDS was MDS with single lineage dysplasia accounting to 46% of the cases. Followed by MDS EB-2 in 23% other cases. This is in concordance with other studies, probably because bigger number of refractory anemia studied showed no significant dyspoiesis in any of the lineages.

In our study, one patient had previous history of breast carcinoma attributing to therapy related MDS. During the course of the study two cases with peripheral blood showing 8-10% of blasts, turned out to be acute leukaemia on bone marrow aspiration and flow cytometry. So we could not ascertain whether MDS to AML or denovo AML and so excluded from the study.

Cytogenetic alteration has a prognostic impact. In study done by Abdel et al., all the patients had chromosomal abnormalities. More than 50% had chromosomal deletions, and 37% had abnormal karyotype [10]. Deletion 5q was the most common cytogenetic abnormality seen in 4 patients.

MDS with 5q deletion is a specific entity with good prognosis. MDS with isolated 5q deletion cases typically present with persistent anemia that has no other identifiable cause. It can present as refractory anaemia, neutropenia or thrombocytopenia. However, the most common cytopenia in patients with 5q syndrome is anemia. They present with a striking macrocytic anemia and are generally transfusion dependent [11].

In our study one case with 5q deletion was therapy related MDS which proved to have poor prognosis with death in 4 yrs of diagnosis. One case of 5q deletion had progressed to AML at the time of diagnosis, may be delayed presentation to hospital in Indian scenario. Two other cases showed 5q deletion with deletion 20q was lost to follow up and other with trisomy 8 responded to therapy. Two other cases of 5q deletion responded well to therapy and one was lost to follow up.

As expected patients with MDS EB-2 had highest IPSS-R scoring with poor prognosis. Unusual fact in our study was one case of 5q deletion had progressed to AML and so had high IPSS-R scoring.

We followed the risk stratification using IPSS-R supplemented by molecular testing and categorised the patients into lower, intermediate and high risk. Treatment involved multidisciplinary approach [2]. Patients with lower risk and ICOUS were given PRBC, erythropoietin and thrombopoietin. Patients with lower risk who had persistent cytopenias were given lenalidomide. Patients with high risk were given demethylation agent like decitabine and supplemented with PRBC and hematopoietic growth factors. Patients with 5q deletion were given lenalidomide.

Out of the 50 cases, 21 cases were lost to follow up and hence were not evaluated. Thirteen cases responded to multidisciplinary treatment given and improved. Three cases of MDS EB-1 AND MDS EB-2 showed good response to decitabine therapy in the initial years of follow up. In our study out of 50 cases, six patients died in course of the disease. In total of 11 MDS EB-1 and MDS EB-2 cases 4 patient's death was noted and showed significant risk of association for poor outcome in concordant with other studies Chaubey et al. [12] and Narayanan [1].

5. CONCLUSION

This study attempts to discuss spectrum of patients ranging from refractory anaemia to pancytopenia, categorised from ICOUS to MDS EB-2 deals with IPSS-R risk stratification, treatment and prognosis. Our study supports MDS EB-1 and MDS EB-2 having significant association with poor outcome. We observed median age of 62 yrs for presentation of MDS with weakness and tiredness as common symptoms. MDS EB-1 and MDS EB-2 together was the second commonest WHO category collaterally having the highest IPSS-R score and worst prognosis. 5q deletion was the common cytogenetic abnormality seen and one case had already progressed to acute myeloid leukaemia at time of diagnosis. Multidisciplinary treatment approach was given to patients with intermediate to good prognosis. However, with majority of the cases having poor follow up it is difficult to arrive at any definite conclusion. Hence we suggest the need of more and larger studies from India to understand the prognosis and treatment effectiveness for patients with MDS.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL CLEARANCE

Ethical clearance has been obtained from the institutional ethical committee.

COMPETING INTERESTS

Author has declared that no competing interests exist.

REFERENCES

1. Narayanan S. Clinical, hematological, and cytogenetic profile of adult myelodysplastic syndrome in a tertiary care center. J Blood Med. 2017;8:21-27.
2. Germing U, Kobbe G, Haas R. Gattermann N: Myelodysplastic syndromes: Diagnosis, prognosis and treatment. Dtsch Arztebl Int. 2013;110(46):783–90.
3. Foran JM, Shammo JM. Clinical presentation, diagnosis, and prognosis of myelodysplastic syndromes. The American Journal of Medicine. 2012; 125(7):6-13.
4. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, Thiele J (Eds.) WHO Classification of tumours of haematopoietic and lymphoid tissues, revised 4th ed, IARC: Lyon, France; 2017.
5. Montalban-Bravo G, Garcia-Manero G. Myelodysplastic syndromes: 2018 update on diagnosis, riskstratification and management. Am J Hematol. 2018;93: 129–147.
6. Rakhee Kar, Seema Rao & Renu Saxena. Myelodysplastic syndromes: Classification and prognostic scoring systems and their applicability in Indian scenario-experience from a tertiary care centre. Hematology. 2009:14(3):145-149.
7. Rameshkumar K, Arumugam M, Samaga LN, Shetty P, Shetty J. Myelodysplastic syndrome among elderly patients with anemia: A Single institutional experience. J Appl Hematol. 2018;9:63-7.
8. Shah NM, Prajapati SG, Adesara RP, Patel AP. An analysis of 30 cases of myelodysplastic syndrome. Indian Journal of Pathology and Microbiology. 2009:52(2):206-209.
9. Steensma PD. Myelodysplastic syndromes current treatment algorithm. Blood Cancer Journal. 2018:8:47,1-7.
10. Abdel WR, AL- Haliq AR, Khasawneh R, Al-Momani A, Aladily TN. Myelodysplastic syndromes in jordan: A study form a large center. Int J Biol Med Res. 2012;3(2):1525-1528.
11. Mona Bargotya, Ankita Mehta, Sarjana Dutt, Harsh Dua, Tejinder Singh. Myelodysplastic syndrome (mds) with isolated 5q deletion ((5q – Syndrome): Report of two cases with review of literature. World J Pathol. 2018;7:1-6.
12. Chaubey R, Sazawal S, Dada R, Mahapatra M, et al. Cytogenetic profile of Indian patients with de novo myelodysplastic syndromes. Indian J Med Res. 2011;134:452-457.

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