Research Article

Profile of myelodysplastic syndrome: A study done at tertiary care centre from south India

Rithika Rajendran[1], Sai Shalini C N[1], D Febe R Suman[1*], Krishnarathnam K[2], Rashmika Rajendran[3], Teena Koshy[4], Suresh S[5]

[1]Department of Pathology, [2]Department of Hematology, [3]CRRI, [4]Department of Human Genetics, [5]Department of Medical Oncology
Sri Ramachandra Medical College and Research Institute, Sri Ramachandra University, Porur, Chennai-600116, Tamil Nadu, INDIA.
Email: dr.rithikarajendran@gmail.com, saishalini_cn14@yahoo.com, febemd@gmail.com, krish57@yahoo.com

Abstract

Introduction: Prognosis of myelodysplastic syndrome (MDS) depends on the cytogenetic profile, blast percentage and cytopenias. This study was intended to categorize MDS patients according to established classifications, scoring systems and to assess mortality, acute myeloid leukemia (AML) transformation and survival. **Materials and Methods:** This is a retrospective cohort study done on 26 completely evaluated and followed up adult de novo MDS patients from July 2009 to June 2015. The demography, hematological profile, classification according to WHO, International Prognostic Scoring System (IPSS) and IPSS-R (Revised) were retrieved from records after ethics committee approval. The results were tabulated in Microsoft Excel and statistically analyzed. **Results:** Male/female ratio was 1.2:1. Females were younger. AML transformation and mortality were high with RAEB-1, RAEB-2, IPSS >2.5 and IPSS-R >6. Comparable with other Indian studies, 53.8% had cytogenetic aberrations of which 21.4% had complex abnormalities. 65.4% were of good prognostic subgroup. Mortality was high in the very poor cytogenetic group. **Conclusion:** AML transformation and mortality were comparable with existing literature. Rare cytogenetic abnormalities of t (5; 17) and t (8; 16) seen can be predictors of leukemia. This study will help in adding to the MDS database as minimal data is available for Indian population.

Keywords: Myelodysplasia, IPSS-R, cytogenetics, myelodysplastic syndrome.

[*]**Address for Correspondence:**
Dr. D Febe Renjitha Suman, Professor, Department of Pathology, Sri Ramachandra Medical College and Research Institute, Sri Ramachandra University, Porur, Chennai-600116, Tamil Nadu, INDIA.
Email: febemd@gmail.com

Received Date: 25/06/2015 Revised Date: 04/07/2015 Accepted Date: 06/07/2015

Access this article online

Quick Response Code:

Website: www.statperson.com

DOI: 08 July 2015

INTRODUCTION

Myelodysplastic syndromes (MDS) comprise a group of hematologic disorders with varying presentations which may respond to specific therapy or may evolve into acute leukemia. However patients most commonly present clinically with features of anemia. Peripheral cytopenias and dyspoietic marrow are the primary laboratory features. Various cytogenetic aberrations are commonly seen and are of prognostic importance. French-American-British (FAB) classification groups MDS into five categories[1], while WHO classifies MDS into seven groups[2,3]. Prognosis of the patients has been assessed earlier by the International Prognostic Scoring System (IPSS) which groups patients into four risk categories[4]. As hemoglobin, absolute neutrophil count and platelet count were found to be significant in the prognosis, the Revised International Prognostic Scoring System (IPSS-R) was devised in 2012, grouping MDS patients into five risk categories[5]. Due to socioeconomic constraints, complete evaluation of MDS patients, prognostic grouping, treatment and follow up in Asia and particularly in India is difficult. Hence the available data on Indian patients is limited. With this background, this study was intended to assess the clinico-pathologic profile of MDS patients, group them according to WHO classification and IPSS and IPSS-R prognostic subgroups and assess the treatment outcome in terms of AML

How to site this article: D Febe R Suman *et al.* Profile of myelodysplastic syndrome: A study done at tertiary care centre from south India. *International Journal of Recent Trends in Science and Technology.* July 2015; 15(3): 606-609 http://www.statperson.com (accessed 10 July 2015).

transformation and mortality. The data was compared with existing publications.

MATERIALS AND METHODS

This was a retrospective cohort study done in the Department of Pathology, Sri Ramachandra Medical College and Research Institute, Chennai, South India. The Institutional Ethics Committee approved this study. All adult MDS patients diagnosed and treated between July 2009 and June 2015 were included in the study. Pediatric patients, patients who had prior chemotherapy, radiation or occupational exposure and patients who declined cytogenetic workup and treatment from our centre and of foreign nationality were excluded from the study. The following demographic and laboratory data were collected: age, sex, basic hematology features, peripheral blood film report, bone marrow morphology and blast count, bone marrow biopsy report, cytogenetics, treatment and prognosis in terms of AML transformation and mortality. The bone marrow aspirate and biopsy were reported with the consensus of three pathologists as per the department policy. Chromosomal analysis was done for at least 20 metaphases and karyo typing was performed according to the International System for Human Cytogenetic Nomenclature (ISCN 2005). IPSS and IPSS-R scoring was done based on the available data. The patients were treated as per standard MDS protocol, MDS with 5q deletion syndrome protocol and on conversion to acute myeloid leukemia (AML) with standard AML protocol. The patients were followed up till June 2015. The data was entered in Microsoft Excel 2007 and statistical analysis and chi square test was done with IBM SPSS statistics 19 software. The overall survival of the entire cohort and the different WHO subtypes, IPSS risk groups and IPSS-R risk groups and cytogenetic prognostic groups were assessed using the Kaplan-Meier method. P value of less than 0.05 was considered significant. For comparison of data, scientific publications on MDS were used.

RESULTS

Twenty six patients were included in the study. Male-female ratio was 1.2:1. The mean age of the patients was 56.7±15.3 years ranging from 25 years to 80 years. Females were younger with a mean age of 49.8±16.7 years ranging from 25 years to 70 years. The mean age of males was 62.6±11.5 years ranging from 42 years to 80 years. 11.5% of the patients were below 30 years and were all females. The hematological values at presentation were mean hemoglobin of 7.8±2.2 g/dL ranging from 3.4 g/dL to 11.3 g/dL, mean total white blood cell (WBC) count of 6863.5 ±7632.5 cells/mm³ ranging from 1180 cells/mm³ to 38300 cells/mm³. The mean absolute neutrophil count was 1.6 ±1.4x10³ cells/mm³ ranging from 0.05 x10³ cells/mm³ to 6.2 x10³ cells/mm³ and the mean platelet count was 1.2 ±1.3 $x10^5$/mm³ ranging from 0.15 $x10^5$/mm³ to 5.8 $x10^5$/mm³. The females were more anemic (7.2 ±1.9 g/dL) and thrombocytopenic (0.9 ±0.6 $x10^5$/mm³) than male patients (hemoglobin 8.4 ±2.2 g/dL; platelets 1.5 ±1 $x10^5$/mm³).

Table 1 shows the demographic and hematological pattern of the patients, classification according to WHO, IPSS and IPSS-R scoring. Cytogenetics, AML transformation and mortality were also included.

WHO classification: Patients with MDS del (5q) were above 65 years of age and male/female ratio was 1:2, with survival ranging from 36 to 49 months since diagnosis. More number of patients were seen in refractory cytopenia with multilineage dysplasia (RCMD) and refractory anemia with excess blasts-2 (RAEB-2) (23.1% in each). The mortality was high in RAEB- 1 (50%) and RAEB- 2 (33.3%). 50% of the RAEB- 2 patients transformed into acute myeloid leukemia and 25% of the RAEB- 1 patients died of acute myeloid leukemia.

IPSS score: More cases were noted in the intermediate-1 risk category, comparable to a study from Singapore[6]. Acute leukemia transformation was seen in intermediate-2 (16.7%) and high risk (40%) category. One patient of intermediate-1 risk (8.3%) died of AML. The mortality was high in intermediate-2 (33.3%) and high risk (20%) categories. The survival in low risk group was high, ranging from 27 to 49 months. There was a significant difference in the mortality and AML transformation between the IPSS risk categories.($p=<0.05$)

IPSS-R score: The number of patients in the intermediate and very high risk categories were more (26.9% each). Acute leukemia transformation was seen with very high risk group only (42.9%). Mortality was seen in intermediate (14.3%), high (20% - AML) and very high risk (28.6%) categories.

Cytogenetic prognostic group: 53.8% (14 patients) had cytogenetic aberrations of which 21.4% had complex abnormalities[7]. 65.4% were of good prognostic subgroup and isolated 5q deletion was noted in 11.5%. The other chromosomal abnormalities were monosomy 7 (3.8%), trisomy 8 (7.7%), deletion 20q (7.7%) and deletion 11q (3.8%). The rare aberrations noted in the study were t(5;7) and t(8;16). Mortality was high in the very poor cytogenetic group. Two patients (11.8%) of good cytogenetic prognostic subgroup died of which one had AML transformation.

Table 1: Clinico-pathologic profile of MDS patients

No	AGE	SEX	Hb	TC	ANC	Plt	WHO	IPSS	IPSS-R	KARYOTYPE	OUTCOME (Duration in months)
1	58	F	8.1	3300	1	0.9	RCMD	1.5	5.5	Monosomy 7	Alive (20)
2	56	F	3.4	7100	1.3	0.2	RCMD	1.5	5.5	Trisomy 8	Alive (20)
3	26	F	7.2	6500	1	1.5	RCMD	3	7	Complex karyotype	Alive (17)
4	58	M	7.5	38300	0.6	0.6	RCUD	3	8	46,XY,t(5;17)[64%]/ 46,XY[36%]	Alive (16)
5	57	M	9.1	7200	6.2	0.9	RAEB-2	3	9	46,XY[56%]/ 47,XY,+8[44%]	AML M6 (15)
6	25	F	6.9	10500	0.6	0.45	RAEB-2	2.5	8	46,XX,t(8;16)	AML M4/5 (17)
7	50	F	8.6	20800	0.1	1.5	RAEB-2	2	5.5	46,XX	AML M1 (18)
8	57	M	8.4	2300	1.1	0.3	RCMD	0.5	4	46,XY	Alive (15)
9	55	M	6.8	2500	1.6	0.3	RCUD	0	3.5	46,XY	Alive (29)
10	43	F	8.1	3110	1.5	1.96	RAEB-2	1.5	5	46,XX, del (20q)	Alive (32)
11	68	M	11	4600	1.9	1.64	RAEB-1	0.5	3	46,XY	Alive (28)
12	69	M	7.1	1600	0.6	0.9	RAEB-2	3	9.5	Complex karyotype	Died (2)
13	66	M	11	3700	0.2	2.14	RCUD	0	1.5	46,XY	Alive (50)
14	80	M	7.2	3700	1.2	1.5	MDS del(5q)	0.5	2.5	46,XY,del (5q)	Alive (40)
15	65	F	6.4	8630	3.6	0.6	MDS del(5q)	0.5	3	46,XX,del (5q)	Alive (38)
16	69	M	5.6	1180	0.2	0.45	MDS-U	0.5	3.5	46,XY,del(20q)	Alive (39)
17	27	F	6.6	4300	2.1	0.36	RCUD	0.5	3.5	46,XX	Alive (26)
18	42	M	11	9840	3.1	5.82	RCMD	0	0	46,XY,del(11q)	Alive (50)
19	80	M	3.7	2280	0.5	0.15	MDS-U	0.5	5	46,XY	Alive (17)
20	64	M	8.2	4100	0.9	0.9	RCMD	0.5	2.5	46,XY	Alive (50)
21	68	F	11	4200	1.5	1.05	RAEB-2	2	4	46,XX	Died (32)
22	45	F	6.9	1900	1.6	0.37	RAEB-1	1	5.5	46,XX	Died (AML M2) (36)
23	70	F	4.6	5400	3.2	1.19	MDS del(5q)	0.5	3.5	46,XX,del(5) (q14>q33)	Alive (51)
24	43	M	11	4330	2.3	1	RAEB-1	0.5	3	46,XY	Alive (50)
25	68	M	10	5760	0.7	4.2	RAEB-1	1.5	6.5	Complex karyotype	Died (15)
26	65	F	8.6	11320	3.7	0.46	RCUD	0.5	4	46,XX	Alive (70)

DISCUSSION

There was a slight male preponderance in the present study like many other earlier reports from various countries [8]. The mean age was higher than the earlier Indian studies; however one study had included patients less than 18 years as well[9,10]. Studies from Asian countries have shown a comparable mean age as ours[11-13]. In this study females were younger than males, amongst whom 25% were younger than 30 years. The disease is more prevalent in older age groups in the Western world[7]. The reason for MDS occurring in younger populations in Asian countries, more so in females, needs to be researched on the grounds of early clonal aberrations. Anemia and thrombocytopenia were more severe among females; though the severity of anemia can be attributed to probable nutritional causes, the reason for more severe thrombocytopenia along with anemia may be due to more severe bone marrow changes which need to be researched further. When the MDS patients were grouped according to WHO classification, AML transformation and mortality were higher with RAEB 1 and RAEB 2. The same observations were made by earlier studies [14]. 11.5% had MDS associated with isolated del (5q) which is lower than the earlier reports from other countries but comparable with a study from India[15,10]. The survival up to follow up period was also higher with a range of 36 to 49 months. Earlier studies also show a similar favorable prognosis in MDS associated with isolated del (5q) [14,16]. They belonged to intermediate- 1 risk in IPSS and low and intermediate category in IPSS-R. The risk category is slightly higher when compared to earlier studies. The AML transformation is comparable with Asian studies [9]. As per the IPSS-R prognostic scores, acute myeloid leukemia transformation was seen in high (died) and very high risk. Mortality was seen in patients belonging to intermediate to very high risk groups. The prognosis decreased from very low risk to very high risk groups. Cytogenetic aberrations were noted in 53.8% of our patients. Two reports from India are comparable to our study (47.5% and 54.48%) while the other two are not comparable (37.5% and 88%) [9,10,17]. The common aberrations are 5q deletion and complex karyotype. While the most common abnormality was monosomy7 in an Indian study, however the percentage of 5q deletion is higher than ours [10]. Other studies from Asian countries were also comparable to ours. The patients with complex

karyotype are two males of 68 and 69 years and a young female of 26 years. The male patients were grouped under RAEB- 1 and RAEB- 2 (WHO), with IPSS score of 1.5 and 3 and IPSS-R scores are 6.5 and 9.5. Both the patients died at 15 and 2 months of diagnosis respectively without AML transformation. This is comparable with other studies [14]. The female patient was in RCMD (WHO), with IPSS score of 3 and IPSS-R score of 7. This patient is alive for 15 months with treatment till the end of the study. The complex karyotype is associated with bad prognosis with regard to mortality and duration of survival. The rare anomalies seen are t (5;17) and t (8;16) which are frequently found in acute leukemia. The patient with t (8;16) transformed into acute leukemia in 3 months. The patient with t (5;17) survived till the end of the study (20 months). AML transformation occurred in 4 patients (15.4%) of whom the cytogenetic profiles are trisomy 8 (AML M6 in one month), t(8;16) (AML M4 in 3 months) and normal karyotype (AML M1 in 3 months and AML M2 in 24 months). The percentage of mortality in our study is 15.4% of which one patient died of AML, two had complex karyotype and one was in RAEB- 2 subgroup. Our study has the limitations of smaller number of patients in certain subgroups limiting comparability and short duration of follow up of some patients who had been diagnosed recently.

CONCLUSION

The patients of MDS in our study were younger and females were younger than the males. Anemia and thrombocytopenia were more severe in females than males. The possibility of MDS needs to be ruled out in this population. MDS with isolated del (5q) had a good prognosis and RAEB- 1 and RAEB- 2 had bad prognosis. The prognosis from low risk to high risk IPSS category is worsening. Similarly the prognosis worsened from very low risk to very high risk IPSS-R category. Patients with complex karyo type had bad prognosis. This study will contribute in adding to the database of MDS and will help in the revision of prognostic scoring systems in future. The reason for younger patients developing MDS needs to be researched further.

REFERENCES

1. Bennett JM, Catovsky D, Daniel MT, et al: Proposals for the classification of the myelodysplastic syndromes. Br J Haematol 51:189–199, 1982.
2. Vardiman JW, Thiele J, Arber DA, et al: The 2008 revision of the World Health Organization (WHO) classification of myeloid neoplasms and acute leukemia: rationale and important changes. Blood 114:937-951, 2009.
3. Haus O, Kotlarek-Haus S, Potoczek S, et al: Myelodysplastic syndromes according to FAB and WHO classification. Single center experience. Neoplasma 53:136-143, 2006.
4. Greenberg P, Cox C, LeBeau MM, et al: International scoring system for evaluating prognosis in myelodysplastic syndromes. Blood 89:2079–2088, 1997.
5. Greenberg P, Tuechler H, Schanz J, et al: Revised international prognostic scoring system for myelodysplastic syndromes. Blood 120:2454–2465, 2012.
6. Lau LG, Chng WJ, Liu TC, et al: Clinico-pathological analysis of myelodysplastic syndromes according to French-American-British classification and International Prognostic Scoring System. Ann Acad Med Singapore 33:589-595, 2003.
7. Schanz J, Tüchler H, Solé F, et al: New comprehensive cytogenetic scoring system for primary myelodysplastic syndromes (MDS) and oligoblastic acute myeloid leukemia after MDS derived from an international database merge. J Clin Oncol 30:820–829, 2012.
8. Belli C, Acevedo S, Bengio R et al: Detection of risk groups in myelodysplastic syndromes: A multicenter study. Haematologica 87:9-16, 2002.
9. Vundinti BR, Kerketta L, Jijina F, et al: Cytogenetic study of myelodysplastic syndrome from India. Indian J Med Res 130:155–159, 2009.
10. Chaubey R, Sazawal S, Dada R, et al: Cytogenetic profile of Indian patients with de novo myelodysplastic syndromes. Indian J Med Res 134:452–457, 2011.
11. Oguma S, Yoshida Y, Uchino H, et al: Clinical characteristics of Japanese patients with primary myelodysplastic syndromes: a co-operative study based on 838 cases. Leuk Res 19:219-225, 1995.
12. Tien HF, Wang CH, Chuang SM, et al: Cytogenetic studies, ras mutation and clinical characteristics in primary myelodysplastic syndrome: a study on 68 Chinese patients in Taiwan. Cancer Genet Cytogenet 74:40-49, 1994.
13. Intragumtornchai T, Prayoonwiwat W, Swasdikul D, et al: Myelodysplastic syndromes in Thailand: a retrospective pathologic and clinical analysis of 117 cases. Leuk Res 22: 453-60, 1998.
14. Malcovati L, Porta MGD, Pascutto C, et al: Prognostic factors and life expectancy in myelodysplastic syndromes classified according to WHO criteria: A basis for clinical decision making. J Clin Oncol 23:7594-7603, 2005.
15. Haase D: Cytogenetic features in myelodysplastic syndromes. Ann Hematol 87:515-526, 2008.
16. Chen B, Zhao WL, Jin J et al: Clinical and cytogenetic features of 508 Chinese patients with myelodysplastic syndrome and comparison with those in Western countries. Leukemia 19:767-775, 2005.
17. Kadam P, Dadabhoy K, Bhisey A et al: Chromosome investigations and clinical outcome in patients with myelodysplastic syndromes. Indian J Med Res 101:163=9, 1995.

Source of Support: None Declared
Conflict of Interest: None Declared