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Clinical Haematology

Study of Morphological and Cytogenetic Profile of Patients with Acute Myeloid Leukemia in Kashmir Valley

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Abstract: Acute myeloid leukemia (AML) is a quickly progressive disease of the myeloid lineage of blood cells. It occurs more commonly in adults than in children, and more commonly in men than women. .While a presumptive diagnosis of AML can be made by examination of the peripheral blood smear when there are circulating leukemic blasts, a definitive diagnosis usually requires an adequate bone marrow aspiration, biopsy and flowcytometry. Cytogenetics study is important in classification of AML and plays an important role in determining the prognosis of the disease. Aim of the study was To study the morphological and cytogenetic profile of AML patients in kashmiri population. This was a retrospective study conducted at Sher-i-Kashmir Institute of Medical Science, Srinagar in the Department of Clinical Hematology on the patients diagnosed as AML patients from January' 2013 to May' 2017. The patient data was collected from Regional Cancer Centre. The clinical history, baseline investigations and other specific investigations like bone marrow examination and immunophenotyping was recorded on a preformed proforma. SPSS software was used for statistical analysis. Out of the total 138 cases, 71 were males (51.45 %) & 67 were females (48.55 %) of the total cases. The mean age of presentation in males was 14.2 ± 1.92 and in female was 13±1.82. Leukocytosis was seen in 47.01 % of the total cases in which leucocyte data was available. AML- M2 was the predominant type seen in 45.22 %(52 out of 115 cases).48 % of total cases (24 out of 50) in which cytogenetics were carried out were with Abnormal Cytogenetics. t(8,21) was seen in 10 out of 24 cases .In 7 cases with AML-M3 morphology , PML RARA test was carried out and it was positive in 5 cases.

Keywords: AML, cytogenetics, molecular profile.

INTRODUCTION

"Leukemia is a group of cancers that usually begin in the bone marrow and result in high numbers of abnormal white blood cells (blasts) [1]. Acute myeloid leukemia (AML) is a cancer of the myeloid lineage of blood cells. It occurs more commonly in adults than in children, and more commonly in men than women. It is treated with chemotherapy. The five-year survival rate is 40%, except for APL (Acute Promyelocytic Leukemia), which has a survival rate greater than 90%. Symptoms include fatigue, shortness of breath, easy bruising and bleeding, and increased risk of infection. Several risk factors and chromosomal abnormalities have been identified .While a presumptive diagnosis of AML can be made by examination of the peripheral blood smear when there are circulating leukemic blasts, a definitive diagnosis usually requires an adequate bone marrow aspiration, biopsy and flowcytometry. Cytochemical stains on blood and bone marrow smears are helpful in the distinction of AML from ALL, and in sub classification of AML. The combination of a myeloperoxidase or Sudan black stain and a nonspecific esterase stain will provide the desired

information in most cases [2]. A sample of marrow or blood is typically also tested for chromosomal abnormalities by routine cytogenetics or fluorescent in situ hybridization. Genetic studies may also be performed to look for specific mutations in genes such as FLT3, nucleophosmin, and c- KIT, which may influence the outcome of the disease [3]. A large number of molecular alterations are under study for their prognostic impact in AML. FLT3 internal tandem duplications (ITDs) have been shown to confer a poorer prognosis in AML with normal cytogenetics [3]. Two other mutations - NPM1 and biallelic CEBPA are associated with improved outcomes, especially in people with normal cytogenetics [3]. Additional markers(e.g., RUNX1, ASXL1, and TP53) that have consistently been associated with an inferior outcome.

AIMS AND OBJECTIVES

To study the morphological and cytogenetic profile of AML patients in kahmiri population

MATERIALS AND METHODS

This was a retrospective study conducted at Sher-i-Kashmir Institute of Medical Science, Srinagar in the Department of Clinical Hematology on the patients diagnosed as AML patients from January' 2013 to May' 2017..The patient data was collected from Regional Cancer Centre. The clinical history, baseline investigations and other specific investigations like bone marrow examination and immunophenotyping was recorded on preformed proforma.SPSS software was used for statistical analysis.

OBSERVATIONS AND RESULTS

A total of 138 cases were enrolled. Various parameters of patients were studied analyzed during the study period (Table 1,2,3). Total of 138 cases were under study, complete bone marrow data was available for 115 cases equaling 83.33 %. (Table 4)Cytogenteics were carried on 50 cases in which 24 cases showed abnormal cytogentics(Table 5,6) .Molecular profile was available in 96 cases(Table 7)

Table-01: Gender Distribution of AML Patients

PATIENTS	No.	% age	MEAN	± Std. DEVIATION	P-Value
Male	71	51.45	14.2	± 1.92	0.000 (S)
Female	67	48.55	13.4	± 1.82	0.000 (S)
Total	138	100	27.6	± 1.52	0.000 (S)

Table-02:- Demographic Characteristics of All AML Patients

Different Age Groups			Male		Female		Total		P-Value
			No.	% age	No.	% age	No.	% age	
Ag (Yr)	Children	<18	14	19.72	10	14.93	24	17.39	0.001 (S) MALE 0.002 (S) FEMALE 0.000 (S) TOTAL
	Adult	18-60	43	60.56	47	70.14	90	65.22	
	Elders	>60	14	19.72	10	14.93	24	17.39	
		Total	71	100	67	100	138	100	
Age (Yr)	Mean ± SD		7.89 ± 4.68		7.44 ± 4.98		15.33 ± 7.81		

Table-03: Details of Total Leukocyte Count (TLC) of AML Patients

Details		No. of Patients	% age
Complete Data Not Available		21	15.22
Complete Data Available		117	84.78
Total		138	100
Details of TLC		No. of Patients	% age
Details as per Available Data	TLC < 4,000 (Leukopenia)	32	27.35
	TLC = 4,000 – 10,000 (Normal)	30	25.64
	TLC > 10,000 (Leukocytosis)	55	47.01
	Total	117	100

Table-04: Classification of AML Patients, (FAB Classification)

Details		No.	% age	
Complete Data Not Available		23	16.67	
Complete Data Available		115	83.33	
Total		138	100	
Details	Type	No.	% age	P-Value
Data Available	AML-M0	04	3.48	0.000 (s)
	AML-M1	38	33.04	
	AML-M2	52	45.22	
	AML-M3	07	6.09	
	AML-M4	04	3.48	
	AML-M5	06	5.22	
	AML-M6	03	2.60	
	AML-M7	01	0.87	
	Total	115	100	

Table-05:- Cytogenetic Characterization of AML Patients			
Details		No.	% age
Cytogenetics not Done		88	63.77
Cytogenetics Done		50	36.23
Total		138	100
Cytogenetics Done	Normal Cytogenetics	22	44
	Culture Failed/ Less Observable Mata phases	04	08
	Abnormal Cytogenetics	24	48
	Total Cytogenetics Done	50	100

Table-06: Cytogenetic Characterization of AML Patients

Details	Type of Defect		No.	% age
Abnormal Cytogenetics	Defect in Chr. No.	Hypoploidy - with loss of X	02	8.33
		Hypoploidy -with loss of Y	02	8.33
		Hyperploidy -with add. Of X	01	4.17
		Hyperploidy -with add. Of Y	Nil	Nil
		Hyperploidy -with add. Of Chr.	01	4.17
		Normal No.	18	75.00
		Total	24	100
	Defect in Chr. Str.	t(8;21)	02	8.33
		t(15;17)	04	16.67
		t(6;9)	01	4.17
		t(9;11)	01	4.17
		t(1;7)	01	4.17
		t(8;21) with -X	04	16.67
		t(8;21) with -Y	02	8.33
		t(8;21) with -X + del(9)	01	4.17
		t(8;21) with del(9)	01	4.17
		del(5)	01	4.17
		del(11) with + XX	01	4.17
		Inv(16)	01	4.17
		Inv(9)	01	4.17
		Nil	03	12.5
		Total	24	100

Table-07: Molecular Profile of AML Patients

Details				No.		% age	
Complete Data Not Available				42		30.44	
Complete Data Available				96		69.56	
Total				138		100	
Details	Type of test	No. of (+ve) Test	% age	No. of (-ve) Test	% age	Total	% age
Data Available	FLT	07	18.42	31	81.58	38	100
	NPM	13	50.00	13	50.00	26	100
	CEBPA	zero	zero	17	100	17	100
	BCR-ABL	01	12.5	07	87.5	08	100
	PML-RARα	05	71.4	02	28.5	7	100
	Total	26	27.08	70	72.92	96	100

DISCUSSION

A total of 138 cases were enrolled. Out of the total 138 cases, 71 were males equaling 51.45 % & 67 were females equaling 48.55 % of the total cases. 17.39 % of the cases were children of both the sex, of age less than 18 years. 65.22 % of cases were adults of both the sex, of age less than or equal to 60 years. 17.39 % of cases were elders of both the sex, of age above 60 years. The mean age of presentation in males was 14.2 ± 1.92 and in female was 13±1.82, while overall age of presentation was 27.6 ± 1.52. Lima MC [4] *et al*. in their study on 51 patients, found 55% (n = 28) were males and 45% (n = 23) females, at a ratio of 1.2:1.Mean age at diagnosis was 7.3 years (SD ± 4.8 years) witha median of 9 years. Udayakumar AM *et al*. [5] in their study found 41 were male and 22 female with median age at diagnosis was 25 years. Total of 138 cases were under the study, data of Total Leukocyte Count (TLC) was available in 117 cases (84.78 %). Out of 117 cases 32 showed Leukopenia (27.35 %), 30 cases were with normal TLC (25.64 %) and 55 out of 117 cases showed Leukocytosis 47.01 %). In a study by Lima MC *et al*. [4] 47% of cases had WBC count>10000/ul. Out of 115 cases with available Bone Marrow data. AML- M2 was the predominant type seen in 52 cases (45.22%. 38 cases of AML-M1 i.e. 33.04 % were seen. Udayakumar AM *et al*. [5] in his study also found M2 subtype as the most frequent subtype (22 of 63; 35%). Raina et al. [6] in their study found M2 in 57 % cases. Also, M2 was the most common group seen in study by Chaudry *et al*. [7] in which it accounted for 44.4% .In our study, Cytogentetics data was available in 50 cases. Out of 50 cases, 22 cases (44%) showed Normal Cytogenetics, while 24 cases (48 %)were with Abnormal Cytogenetics. 7 cases with M3 morphology were tested for PML-RARα.05 cases were (+ve) for PML-RARα (71.4%).Isolated t(8;21) was seen in 8.33 %,. While as 04 cases showed translocation t(8;21) with loss of X-Chromosome (16.67 %), 02 cases showed translocation t(8;21) with loss of Y-Chromosome (8.33%). Molecular profile was available in 96 cases (69.56 %).Out of 96 cases, in 38 cases test for FLT was done (39.58%). Out of 38 cases 07 cases were (+ve) for FLT (18.42 %).Out of 96 cases NPM test was done only in 26 cases (27.08 %). Out of 26 cases, 13 cases (50%) were with (+ve) NPM test. CEBPA was done in 17 cases (10.42 %). All the cases were negative. In a study by Udayakumar AM *et al*. [5] Chromosome abnormalities were present in 39 of 63 patients (62% overall, or 44% for adults and 18% for children). Lima MC *et al*. [4] in their study on 51 patients, found chromosomal alterations in 46.15% of cases. The literature reports that the translocation t(8;21) is the most prevalent, varying between 12% and 23% [8-10], whereas t(15;17)is observed in 3.4---10% of cases [8,10], Lima MC *et al.* [4] in their study found that The most frequent alteration was t(15;17), foundin six patients (23%) . In a study by Sazawal S *et al.* [11] Fifty five (96.5%) of the 57 patients classified as having APL were positive for PML-RARα, AML1-ETO was detected in 16 of 56 patients. Udayakumar AM *et al*. [5] in their study found that Balanced translocations, t(8;21) and t(15;17) were observed in 7 of 63 (11%) and 6 of 63 (10%), respectively.

CONCLUSION

AML involves males more than females. Adults have higher % age (65.22 %) of occurrence as compared to children below 18 years age & elder above 60 years of age both with same % age (17.39 %) of the cases.AML- M2 was seen in majority of cases (45.22%).Abnormal cytogenetics were seen in 48% of cases.

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