THE ROLE OF IMMUNE RESPONSES IN THE PATHOGENESIS OF MYELODYSPLASTIC SYNDROMES.

Hashem Mohamed Neaanaa, Nabil Ahmed El Halawani, Zeinab Ibrahim Mourad,* Dalia Ahmad Nafea, Raitha Rashid Suleiman

Department of Internal Medicine – Hematology Unit, Department of Clinical and Chemical Pathology,* Faculty of Medicine, Alexandria University

INTRODUCTION

Myelodysplastic syndromes (MDS) are characterized by ineffective hematopoiesis with blood cytopenias, morphological dysplasia and has tendency to progress into AML. MDS is regarded as the most prevalent form of acquired bone marrow failure syndrome in older adults > 65years of age and more common in men than in women. The current 2022 WHO classification introduces the term myelodysplastic neoplasms (abbreviated MDS) to replace myelodysplastic syndromes. The cause of MDS still remain unknown, however the etiology can be categorized into MDS arise without any underlying cause as de novo in older patients, or with underlying cause as secondary MDS.

The hallmark of MDS pathogenesis is dysregulated hematopoietic differentiation which result in impaired differentiation, morphological dysplasia, and cytopenia, and all of these are due to complex interplay between genetic and epigenetic alterations, bone marrow microenvironment, and the immune system. Therapeutic options for adult patients with MDS vary from supportive care to allo-HCT.

AIM OF THE WORK

The aim of the present study was to assess and evaluate the role of the immune responses in the pathogenesis of MDS by measuring some of the cytokines levels include IL-10, IL-6, IL-2, TNF-α, as well as CD4, CD8 and CD4/CD8 ratio in MDS patients.

PATIENTS AND METHODS

This prospective study was conducted on 11 newly diagnosed cases of MDS patients and 20 healthy as control (Egyptians) in Haematology Unit at Alexandria Main University Hospital and clinics between September 2020 and May 2022. Patients and controls were matched in the demographic criteria in the form of age (18 - 65years) and sex. The study was approved by the local Institutional Review Board, and informed consent was obtained from all study participants. Detailed clinical history and physical examination was obtained and fresh blood samples were collected from every participant. The expressions levels of some cytokines include serum IL-2, IL-6, IL-10 and TNF-α were evaluated by ELISA, while the flow cytometry done to determine the expression of CD4, CD8 and CD4/CD8 ratio.

RESULTS

Table 1: Comparison between the two studied groups regarding laboratory investigations.

Parameters	MDS cases		Control		Test of significance
	Mean SD	Min - Max	Mean SD	Min - Max	
WBC (x 10^3µ/L)	2.02±1.12	0.88 - 4.02	6.08 ± 1.8	4.08 - 10.56	Z = 4.54 p < 0.001*
ANC (/ µL)	0.73±0.51	0.23 - 1.75	3.57 ± 1.25	2.03 - 7.13	Z = 4.54 p < 0.001*
Hb (g/dL)	6.95±1.45	4.6 - 8.9	13.4 ± 1.25	12 – 16	Z = 4.54 p < 0.001*
PLT (x 10^3µ/L)	98±52.6	30 - 168	247 ± 45.9	151 – 356	Z = 4.46 p<0.001*
Serum. IL-10	74.81±50.48	8.86 – 161.32	27.03±16.87	10.88 – 77.33	Z = 2.66 p < 0.008*
Serum IL-6	44.72±4.24	40.28 – 54.01	43.61±3.47	39.11 – 51.06	Z = 0.764 p < 0.435
Serum.IL-2	48.06±29.03	16.49–107.13	20.47±7.17	14.45 – 46.80	Z = 3.180 p < 0.001*
TNF-α	34.75±22.23	8.38 – 61.08	12.32±3.92	6.52 – 19.93	Z = 2.768 p < 0.006*
CD4 (%)	39.36±15.17	23.00 – 74.00	41.05±7.41	26.00 – 54.00	t = 0.347 p < 0.735
CD8 (%)	27.82±12.91	13.00 -58.00	29.80±6.43	18.00 – 43.00	t = 0.477 p < 0.64
CD4/CD8ratio	1.73±1.33	0.60 – 5.30	1.46±0.54	0.74 – 3.00	t = 0.637 p < 0.53

Table 2: Comparison between low risk and high risk MDS patients on cytokines level and BM blasts %.

Parameters	LR - MDS patients (n=4)		HR – MDS patients (n=7)		Test of significance.
	Median	Min- Max	Median	Min-Max	
BM blasts %	4.00	3.00 – 4.00	10.00	7.00 – 16.00	p < 0.007*
Serum IL-10	53.95	8.86 - 62.27	76.18	11.12-161.32	p < 0.131
Serum IL-6	41.95	40.28 - 42.15	44.21	42.69 - 54.01	p < 0.008*
Serum IL-2	33.16	24.75 - 74.93	57.95	16.49- 107.13	p < 1.00
TNF-α	21.69	8.38 - 23.46	57.91	10.06- 61.08	p < 0.131
CD4	25.50	23.00- 40.00	42.00	29.00 - 74.00	p < 0.038*
CD8	24.00	21.00 - 38.00	23.00	13.00 - 58.00	p < 0.925
CD4/CD8ratio	1.08	0.80- 1.20	2.17	0.60 - 5.30	p < 0.186

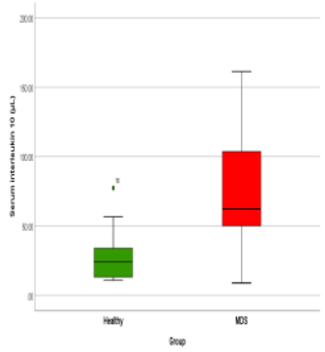

Figure 1:
Box and whisker graph of serum IL-10 (µL) in the studied groups.

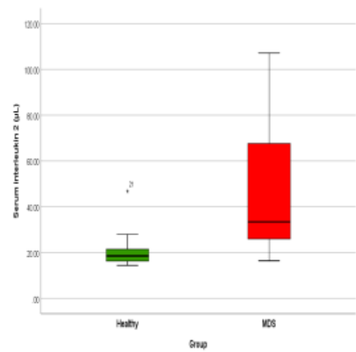

Figure 2:
Box - whisker graph of serum IL-2 (µL)) in the studied groups.

CONCLUSION

The study revealed statistically significant increase levels of serum IL-2, IL-10 and TNF-α, while IL-6, CD4, CD8 and CD4/CD8 ratio were not significantly higher in MDS patients compared to the healthy controls. Regards sub-classification based on risk categories, the serum levels of IL-6, CD4 were statistically significantly higher in high-risk group in comparison to low-risk MDS patients, and the rest includes IL-2, IL-10, TNF-α, CD8 and CD4/CD8 ratio were not significantly higher in HR-group compared to LR-group.

Additionally, significant correlations between age and IL-2, platelet and IL-10, haemoglobin and IL-6 as well as CD4 in MDS patients were demonstrated.