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Original Article

A nationwide non-interventional epidemiological data registry on myelodysplastic syndromes in Lebanon

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Abstract: Myelodysplastic syndromes (MDS) are a heterogeneous group of clonal hematopoietic disorders characterized by peripheral blood cytopenias, blood cells dysplasia, and increased risk for progression to acute leukemia. Physicians should be vigilant in diagnosing MDS and should be aware of the contemporary therapies that are always in progress. Most of the data on MDS epidemiology and management comes from developed countries. The incidence and features of MDS in the Arab countries, among them Lebanon, are not known. We undertook a nationwide epidemiological registry study of all newly diagnosed MDS cases through 2010-2011. Patients were referred by 21 hematologists/oncologists practicing in 17 hospitals and medical centers distributed across the entire country. 58 patients (29 males and 29 females) with confirmed MDS were included. The calculated incidence rate of MDS was 0.71 per 100,000 people. The median age at diagnosis was 73 years (range 16-86). The most common complaints on presentation were fatigue (70.7%), weakness (60.3%) and pallor (43.1%). Most patients were diagnosed as refractory anemia with excess blasts (RAEB; 36.2%) and refractory cytopenia with multilineage dysplasia (RCMD; 32.8%). This paper constitutes the first epidemiological report on the incidence and specific subtypes of MDS in Lebanon.

Keywords: Myelodysplastic syndromes, features, epidemiology, registry, diagnosis, Lebanon

Introduction

Myelodysplastic syndromes (MDS) are a heterogeneous group of clonal hematologic disorders characterized by peripheral blood cytopenias, dysplasia of blood cells, clonal chromosomal abnormalities, and increased risk of progression to acute myeloid leukemia [1, 2]. MDS generally arise *de novo* especially in older patients (primary MDS), or less frequently are secondary to prior chemotherapy or radiotherapy (secondary or treatment-related MDS) [3]. Median age at disease onset is approximately 70 years. Common risk factors for developing MDS include advanced age, male gender, smoking, history of chemo- or radiotherapy, and exposure to agricultural chemicals [4-6].

Although MDS are common, the precise incidence of the disease in developed countries

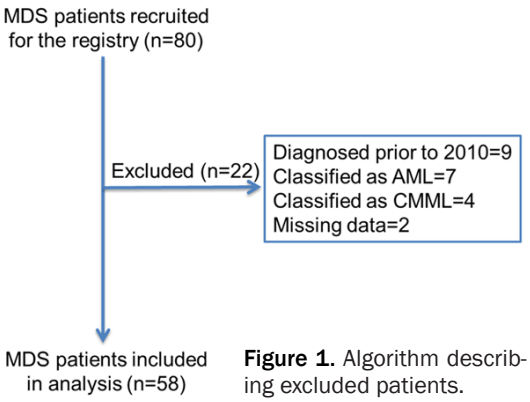

Figure 1. Algorithm describing excluded patients.

Table 1. Initial characteristics of patients

Characteristics	Number (%)
Age (years)	
< 40	3 (5.2)
40-49	3 (5.2)
50-59	5 (8.6)
60-69	6 (10.3)
70-79	29 (50)
≥ 80	12 (20.7)
Gender	
Male	29 (50)
Family history of malignancy	
Yes	3 (5.2)
No	46 (79.3)
Unknown	9 (15.5)
History of radiation exposure	
Yes	2 (3.4)
No	56 (96.6)

has been difficult to estimate. In the United States, cancer registries such as the Surveillance, Epidemiology, and End Results (SEER) registry of the National Cancer Institute (NCI) have only started classifying MDS as neoplastic and capture data on newly diagnosed MDS cases since 2001 [7]. Numbers obtained from insurance claims data have been used to estimate the disease incidence. According to these sources, current estimates are between 30,000 and 40,000 new MDS cases in the United States yearly [8, 9]. The incidence rate of MDS in Europe is estimated at 1.8-2.8 per 100,000 people [10, 11].

Data on the incidence of MDS in the Arab countries is not known, and in Lebanon data is lacking due to the absence of population-based hematologic malignancies registries. Consequently, the clinical and pathological features of MDS cases in Lebanon are not known. We undertook a nationwide initiative to prospectively collect newly diagnosed MDS cases in Lebanon aiming at estimating the annual incidence of this disease and better understand its clinical and pathological characteristics.

Patients and methods

We conducted a prospective nationwide epidemiological data registry on MDS in Lebanon. All adolescent and adult patients diagnosed with MDS during 2010-2011 were eligible for this registry. Institutional Review Board approval was obtained from all participating centers. Signed informed consents were required from enrolled patients. This nationwide collaboration was conducted through the study CRO (ClinServ International). Hematopathology revision of all cases was undertaken by one of our hematopathologists (H.F.).

Patients with a clinicopathological diagnosis of MDS were enrolled. Clinical and pathology data were collected in a data sheet by the principal investigator and co-investigators at the participating centers. The available pathology materials from each patient were reviewed according to the 2008 World Health Organization (WHO) classification system of myeloid neoplasms [12].

Our initial search enrolled 80 patients with MDS. Patients not fulfilling the inclusion criteria and those without enough clinicopathological information to determine the MDS subtype were excluded from the analysis. The selection of patients for analysis was based on the algorithm shown in **Figure 1**. The International Prognostic Scoring System (IPSS) and the revised IPSS (IPSS-R) were calculated as described previously [13, 14]. All data analysis was performed in SPSS software (Version 22, IBM, Armonk, NY, USA).

Results

Our initial search enrolled 80 patients with MDS. However, only 58 patients with confirmed MDS were included in the final analysis. There were 29 (50%) males and 29 (50%) females. The median age at diagnosis was 73 years (range 16-86). These patients were referred by 21 hematologists/oncologists practicing in 17 hospitals and medical centers distributed across the 5 districts in Lebanon.

Table 2. Initial laboratory values on diagnosis

Parameters	Number of cases	Median	Range
WBC	53	4600/μL	1300-18780
ANC	50	2331/μL	280-10906
< 1000/μL	11 (22%)		
< 500/μL	2 (4%)		
AMC	52	270/μL	7-2629
RBC	45	3.26×10^6/μL	1.94-4.43
Hgb	56	9.2 g/dL	4.39-12.8
< 10 g/dL	34 (60.7%)		
< 8 g/dL	12 (21.4%)		
MCV (fl)	48	93	74-114
Platelets	55	101×10^3/μL	12-422
< 100×10^3/μL	26 (47.3%)		
< 50×10^3/μL	10 (18.2%)		
< 20×10^3/μL	3 (5.4%)		
LDH (U/L)	37	183	30-382
Ferritin (μg/L)	32	187	6-2642
Marrow blasts		2%	0-19
> 5%	17 (31.5%)		
> 10%	9 (16.7%)		
> 15%	5 (9.2%)		

Abbreviations: WBC, white blood cell; ANC, absolute neutrophil count; AMC, absolute monocyte count; RBC, red blood cell; Hgb, hemoglobin; MCV, mean corpuscular volume; LDH, lactate dehydrogenase.

Sixteen patients (27.6%) had a history of anemia and 3 (5.2%) had family history of malignancy. The most common complaints on presentation were fatigue (70.7%), weakness (60.3%), pallor (43.1%), fever (12.1%), bruising (12.1%), bleeding (10.3%), and weight loss (10.3%). **Table 1** summarizes the initial characteristics of eligible patients.

At baseline, 49 (84.5%) patients had abnormalities on complete blood count (CBC). The median hemoglobin level for patients was 9.2 g/dL (range, 4.39-12.8 g/dL); most of the patients presented with hemoglobin levels below 10 g/dL (**Table 2**). The median absolute neutrophil count (ANC) for patients was 2.33×10^9/L (range, 0.28×10^9-10.9×10^9/L). The median platelet count was 101×10^9/mm^3.

The median bone marrow blast count recorded at baseline was 2% (range, 0-19%). Erythrodysplasia was the most common observed dysplasia in 45 (77.6%) cases. In 14 (24.1%) patients there was a trilinear dysplasia. Examining the MDS subtypes, most patients were diagnosed as refractory anemia with excess blasts (RAEB; 36.2%) and refractory cytopenia with multilineage dysplasia (RCMD; 32.8%) (**Table 3**). Cytogenetic analysis showed a normal karyotype in 32/53 (60.4%), monosomy 7 in 2/53 (3.8%), complex karyotype in 5/53 (9.4%), chromosome Y deletion in 5/53 (9.4%), trisomy 8 in 3/53 (5.7%), and other abnormalities in 14/53 (26.4%).

When patients were charted according to the calculated IPSS, 24.1% were low risk; 41.4% and 15.5% of patients were in the intermediate-1 and -2 ranges, respectively; and only one patient (1.7%) was high risk. In 10 patients the score could not be calculated due to missing information. When the revised IPSS (IPSS-R) was calculated, 12.1% were very low risk, 34.5% were low risk, 22.7% were intermediate risk, 5.2% were high risk, and 8.6% were very high risk. IPSS-R could not be calculated in 11 patients due to missing information (**Table 4**).

Discussion

Here, we present the first nationwide prospective epidemiological study reporting the incidence and features of MDS in Lebanon. We were able to confirm the diagnosis in 58 patients with MDS who presented in 2010-2011. These patients were managed in 17 hospitals and medical centers distributed across the entire country; these hospitals represent over half of the hospitals in Lebanon.The population of Lebanon was estimated to be 4,100,000 people in 2011. This yields an incidence rate of MDS of 0.71 per 100,000 people. This number is probably an underestimation of the true incidence of MDS in Lebanon if we account for missed cases and patients seen at hospitals other than the ones participating in this study. Taking that into account, MDS incidence in Lebanon is comparable to other countries like Japan (1.6 cases per 100,000 for men and 0.8 cases for women in 2008) [15] and China (1.48 cases per 100,000 for men and 1.54 cases for women) [16]. The incidence in Western countries appears to be higher ranging between 2 and 4 cases per 100,000 [9, 17, 18].

Table 3. MDS subtypes according to 2008 WHO classification

MDS subtype	Number (%)
Refractory anemia (RA)	4 (6.9)
RA with ring sideroblasts (RARS)	7 (12.1)
Refractory cytopenia with multilineage dysplasia (RCMD)	19 (32.8)
Refractory anemia with excess blasts-1 (RAEB-1)	9 (15.5)
Refractory anemia with excess blasts-2 (RAEB-2)	12 (20.7)
MDS associated with isolated del (5q)	1 (1.7)
Myelodysplastic syndrome-unclassified (MDS-U)	6 (10.3)

Table 4. Karyotype, IPSS and IPSS-R of patients

	Number (%)
Karyotype	
Normal	32 (55.2)
Abnormal	21 (36.2)
Uninformative	2 (3.4)
Missing	3 (5.2)
IPSS score	
Low	14 (24.1)
Intermediate-1	24 (41.4)
Intermediate-2	9 (15.5)
High	1 (1.7)
Missing	10 (17.2)
IPSS-R score	
Very low	7 (12.1)
Low	20 (34.5)
Intermediate	12 (20.7)
High	3 (5.2)
Very high	5 (8.6)
Missing	11 (19)

Abbreviations: IPSS, International Prognostic Scoring System; IPSS-R, revised International Prognostic Scoring System.

Characteristics of MDS patients have been shown to vary with ethnicity [19, 20]. Contrary to the general trend of male predominance in MDS, we did not see this gender difference in our study. This appears to be also the case in China [16]. The median age at diagnosis was 73 years which is comparable to that in Europe and the United States [7, 19, 21].

We used the WHO 2008 classification criteria for myeloid malignancies. The most prevalent MDS subtype in our study was refractory anemia with excess blasts (RAEB; 36.2%) followed by refractory cytopenia with multilineage dysplasia (RCMD; 32.8%). We noticed a relatively increased prevalence of RAEB among our patients as compared to published literature [11]. This finding may perhaps be attributed to the late presentation of patients in the course of the disease. This represents an opportunity to educate patients about the manifestations of the disease in order to seek medical attention earlier in the course of the disease. This is important as the prognosis of MDS is significantly worse when the disease is more advanced.

The strength of our study is that we used a nationwide approach encompassing the majority of hospitals in all districts of the country to identify newly diagnosed MDS patients. Most importantly, enrolled cases were reviewed by our hematopathologist to confirm MDS diagnosis and subtyping.

Several limitations of our study should be addressed. Although we only enrolled cases with enough clinicopathological information to determine the MDS subtype, still some cases lacked relevant clinical and laboratory information. We did not intend to assess MDS treatment and outcome during this study. However, we believe that collecting this information is important for a thorough national MDS registry. Another weakness of this study was the lack of a panel of pathologists to be able to render more confirmatory findings.

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Authors' contribution

ZO collected and analyzed the data and wrote the manuscript. NC, ZS, TW, MA, MD, JK, WM, TA, OJ, FF, MW, MH, MK, NB, ME, AK, FK, HY, HK, AT and WS recruited the patients and collected data. NH and RM reviewed and collected the laboratory data. AB designed the study, recruited patients and wrote the manuscript. HF reviewed the hematopathology material. All authors read and approved the final manuscript.

Disclosure of conflict of interest

None.

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