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Research Article

THE EPIDEMIOLOGY OF MYELODYSPLASTIC SYNDROMES RETROSPECTIVE STUDY IN THE HEMATOLOGY DEPARTMENT OF THE MILITARY HOSPITAL OF RABAT

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ABSTRACT

There is no data on myelodysplastic syndrome (MDS) in Morocco. Indeed, this disease has long remained unexplored. We present the epidemiological data on MDS of the department of hematology of the Mohamed V Military Hospital for a period of 9 years and 4 months. In this study, we registered the MDS cases diagnosed by bone marrow examinations between January 2006 and April 2015. We classified these cases according to the 2008 WHO classification. Patients with secondary MDS (post-chemo/radiotherapy were excluded from the analysis. We compiled 155 cases, which is equivalent to 21% of the malign hemopathies recorded on the same period. The median age of diagnosis was 62 years. The group of age under 50 years represented only 8% of the whole study population. There was a preponderance of males with a M/F ratio of 1.58. The distribution according to the WHO subtypes was as follows: refractory cytopenia with multilineage dysplasia (61%) followed by refractory anemia with excess of blasts type 1 (26%) and type 2 (9%). The number of new MDS cases increased through the analyzed period of time. It went from 45 new cases between 2006 and 2011 to 110 new cases between 2012 and the start of 2015. The global frequency of MDS increased over recent years due to the cytologists' increasing awareness of this disease. A national registry is thus imperative in order to estimate the real incidence of MDS in our country and to improve the knowledge on these hemopathies.

KEY WORDS: Myelodysplastic syndrome - Epidemiology.

INTRODUCTION

Myelodysplastic syndromes (MDS) are characterized by clonal myeloid hematological damage to the hematopoietic stem cell causing qualitative and quantitative abnormalities of myeloid lines and progressing to pancytopenia and leukemic transformation [1]. Diagnosis is biological, cytological essentially based on the observation of morphological abnormalities in bone marrow examination. In adults, MDS may appear de novo as they may be secondary in particular to the use of chemotherapeutic agents [2].

The epidemiology of MDS has become a global concern those 10 to 15 years after being integrated by the World Health Organization (WHO) in classification of hematological malignancies which must to be recorded in the cancer registries [3, 4]. However, epidemiological studies are few, since many difficulties are encountered in the exploitation of MDS. First, the International Classification of Diseases Codes has recently recognized the MDS as a distinguished entity from anemia and leukemia. On the other hand, there are no objective diagnostic criteria, and classifications of hematological malignancies and MDS are constantly subject to change. Finally, in 10-20% of cases, MDS are asymptomatic,

leading to an underestimate of the true number of cases. Wu et al work shows that, in many patients, cytopenia appear months or years before the diagnosis of MDS is posed [5].

The term MDS was introduced in 1976 by the FAB group (French-American-British) [6] which ranked them for the first time in several entities by cytologic criteria: refractory anemia (RA), acquired sideroblastic idiopathic anemia (ASIA), refractory anemia with excess of blasts (RAEB), refractory anemia with excess of blasts in "Transformation" (RAEB-t) and chronicle myelomonocytic leukemia (CMML).

This classification has been criticized on several levels. First, it included cytopenia other than anemia in RA. It was also noted that the evolution of the CMML was closer to chronic myeloproliferative disorders, and the RAEB-t approached acute myeloid leukemia.Therefore, WHO has established a new classification (1999, revised 2008) [4, 7], separating the MDS according to the alteration of a single line (refractory cytopenia with unilineage dysplasia [RCUD]) or more lines (refractory cytopenia with multilineage dysplasia [RCMD]), the presence of ring sideroblasts in the Perls staining (refractory anemia with ringed sideroblasts [RARS]), the presence of excess blasts (RAEB 1 or 2), the 5q syndrome and unclassified MDS. By establishing the new category of RCMD, separating the category of RAEB into two classes 1 and 2 and moving the RAEB-t with more than 20% blasts in the category of acute leukemia, and the CMML in border forms with chronic myeloproliferative syndromes, MDS groups have become more homogeneous with better prognostic approach [4, 8]. The classification published in 2008 by WHO has become the reference for diagnosis internationally because it is based on well-defined criteria, more objective and reproducible.

In Morocco, we have not yet National Register of hematological malignancies and little data on MDS exist in the literature. The objective of this work is to study the epidemiological data on MDS in a Moroccan population over a period of 9 years and 4 months.

MATERIAL AND METHODS

This is a retrospective study covering a period of 9 years and 4 months from January 2006 until April 2015. We collected the cases of MDS diagnosed on bone marrow examinations and classified according to the WHO classification while excluding patients with secondary MDS (radiotherapy history and / or antineoplastic chemotherapy). The database (age, gender, date and reason for hospitalization and initial classification) was obtained from registers of the hematology laboratory of Mohamed V Military Hospital Rabat (MVMHR). Patients initially classified according to FAB classification have been reclassified according to WHO classification.

STATISTIC STUDY

Statistical analysis was performed using SPSS software version: 13.0. The results were expressed as numbers and percentages for qualitative variables and means and standard deviations for quantitative variables. The comparisons were made using the appropriate statistical tests: Khi 2 and Fisher exact test; depending on the conditions of use of each test.

Figure 1: Distribution of MDS according to the age groups

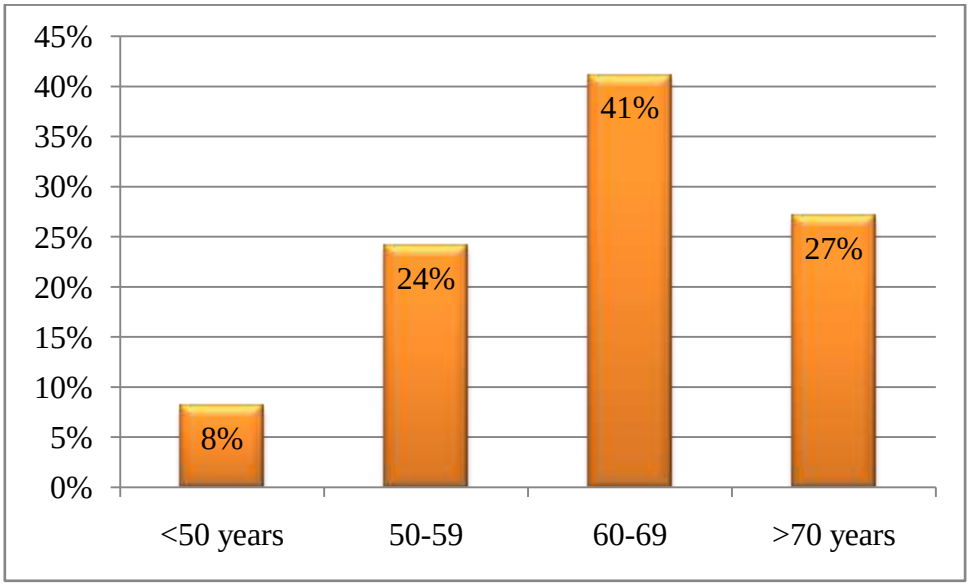


Figure 2: Distribution of MDS according to gender

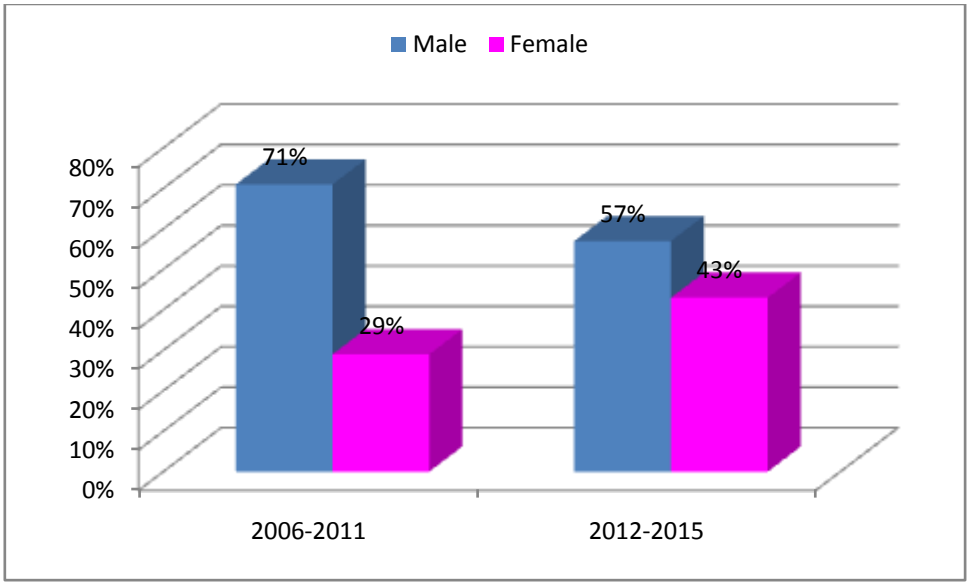
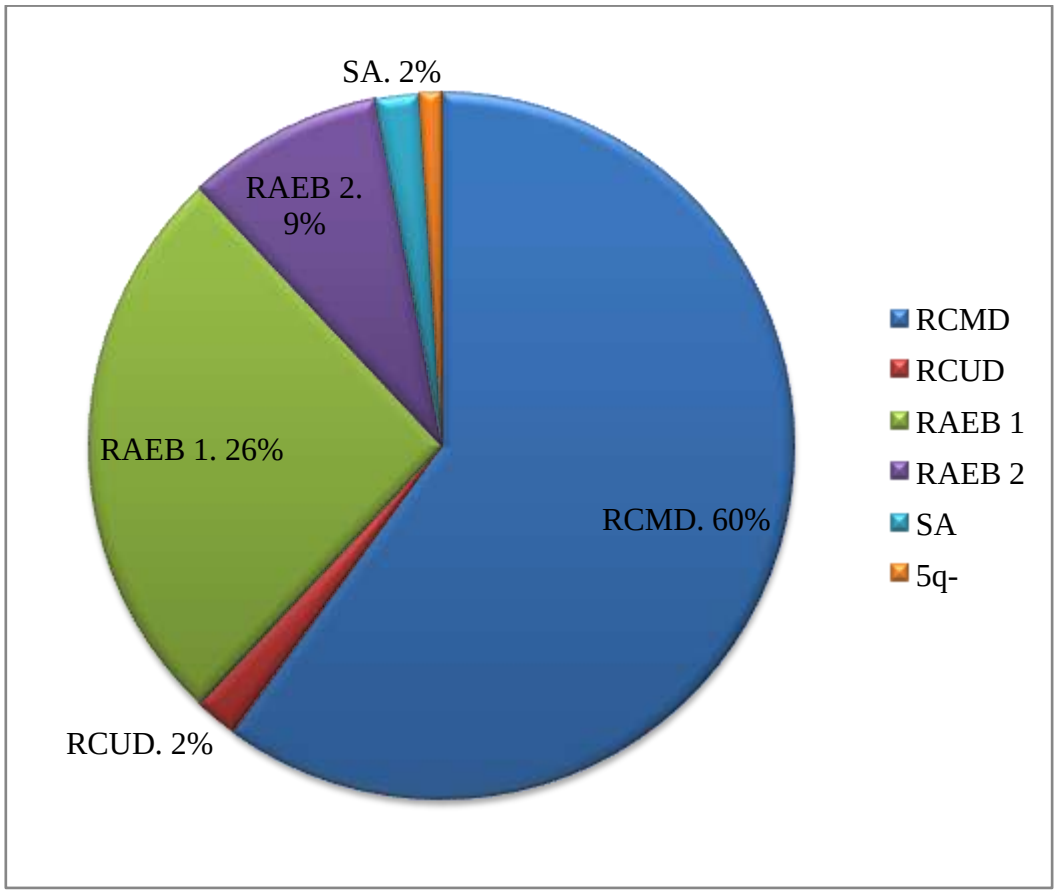


Figure 3: Distribution by subtypes of MDS



RCUD: refractory cytopenia with unilineage dysplasia, SA: sideroblastic anemia, RCMD: refractory cytopenia with multilineage dysplasia, RAEB 1 and 2: refractory anemia with excess blasts 1 and 2, 5q-: 5q deletion syndrome.

Table I: MDS Frequency according to their subtypes and their demographic characteristics

			2006-2011		2012-2015	
	Total	%	Case Number	%	Case Number	%
RCUD	1	0.6	1	2.2	0	0
SA	4	2.6	4	8.9	0	0
RCMD	94	60.6	25	55.5	69	62.7
RAEB1	40	25.8	10	22.3	30	27.3
RAEB2	14	9.1	4	8.9	10	9.1
5q-	2	1.3	1	2.2	1	0.9
Male	95	61.3	32	71.1	63	57.3
Female	60	38.7	13	28.9	47	42.7
< 50 years	13	8.4	4	8.9	9	8.2
50-59	37	23.9	11	24.4	26	23.6
60-69	64	41.2	11	24.4	53	48.2
> 70	41	26.5	19	42.1	22	20

Table II: Summary of findings regarding the mean age and sex ratio according to different studies

AUTHOR COUNTRY (year)	Sex Ratio	Age Average (Year)	Maximum Age	%
Dinmohamed et al. Netherland (2013)	1.49	74	> a 80	25
Ma et al. USA (2007)	1.67	76	70-79	26.8
Neukirchen et al. Germany (2011)	1 .2	71	> a 80	-
Troussard et al. France (2008)	2.04	74	75-79	38
Yahyaoui et al. Morocco (2015)	1.58	62	60-69	41

RESULTS

One hundred and fifty-five new cases of MDS are diagnosed during the period 2006-early 2015, 21% of all hematologic malignancies recorded in the same period. Most patients were from the clinical hematology service of MVMHR (60%). The number of cases of MDS has increased from 45 cases between 2006 and 2011, a rate of 5.5%, to 110 cases between 2012 and the beginning of 2015, a rate of 11.5%.

In over 50% of cases, a single line was initially predominantly affected, the alteration of erythroid line (65/89 cases, 73%). The bicytopenia were the second most common clinical presentation (24.5%) and associate anemia in 90% of cases. Finally, pancytopenia was seen in 18.1% of patients.

AGE DISTRIBUTION

Over the years of the study, the number of patients aged over 60 years was significantly increased ($p = 0.026$). On average, the age of diagnosis was 61.9 years. The age group of 60 to 69 years had a majority (64 cases or 41.3%) followed by over 70 years (41 cases that is 26.5%) and the age group 50 to 59 years (37 cases or 23.9%). Those aged younger than 50 years accounted for only 8.4% of all patients. Over the last four years of the study, the average

age of diagnosis was lower (only 20% of patients were over 70 years) (Figure 1).

DISTRIBUTION BY GENDER

The male was dominant in our series with a sex ratio of 1.58. This ratio was higher during the period 2006-2011 (2.5) compared with the period 2012-early 2015 (1.3) (Figure 2).

Distribution According To Subtypes Of MDS

The RCMD is the predominant class (94 cases, 60.6%) as well in men and women (Figure 3). male subjects having an age of 60 to 69 were the most affected by this category (25 cases, 16.1%). The second most common subtype is the RAEB 1 (26%), followed by the RAEB 2 (9%). The category of RARS ranks third in 2006-2011. Only a case of RCUD and 2 cases of 5q- syndrome were diagnosed over the entire period of the study.

The evolution of subtypes of MDS according to the years of the study is shown in Table I. The frequencies of the main categories have recorded an increase in particular of RCMD which rose from 55.5% in 2006-2011 to 62.7% between 2012 and early 2015. No cases of RCUD or RARS have been registered between 2012 and early 2015. However, 4 cases of RCMD-S (included in RCMD) were diagnosed during this period.

DISCUSSION

We have shown an increase in the number of new cases particularly in the last four years (2.5 times the number of cases reported during the first five years of the study). This fact, noted by other authors, could be explained by aging populations and better diagnosis of this disease, including through the development of the new WHO classification that allowed homogenize subtypes of this disease [9, 10].

MDS is a disease whose frequency increases with age significantly. It is also the most common hemopathy in the elderly [11]. Over the years of the study, we observed a statistically significant increase in the number of patients older than 60 years. Moreover, the average age of diagnosis was not high (61.9 years), which is consistent with the finding reported by Neukirchen. About the average age of diagnosis in African, Asian countries and Turkey (56 years to 61 years) is lower compared to European and North American countries (71 to 76 years old) [12, 13, 14, 15, 16]. Patients older than 80 years accounted for only 6.5% of our entire series. This could be due to the low representation of this age group in our society and the difficult access to hematology specialist services for this category of patients.

It is commonly known that the incidence of MDS is higher among men than women. The sex ratio varies between 1.1 and 2 according to studies (1.58 in our work) (Table II). Most often, the diagnosis is suspected in the clinical signs associated with cytopenia or discovered incidentally during a biological check. Anemia is the most common sign. It is present at diagnosis in 80% of cases and affects 90% of MDS patients at some point in the course of their disease [11].

The alteration of the erythroid cells, with or without other cytopenia, was seen in 83% of patients in our series at diagnosis, which would be another cause of morbidity and mortality, this finding needs to be explored by studies of survival to evaluate its impact on quality of life, the heart function and the physical performance of the patients.

The RCMD were remarkably predominant in our study (60.6%). Neukirchen has found a rate of 31% [12]. RA and RCMD represented almost 50% of cases reported by Troussard [17]. In one Indian study including 40 cases of de novo MDS, the RA were the majority [18]. Finally, in a Dutch study, the rate of unclassified MDS was the most important (49%) [9]. The comparison of the frequencies of different subtypes with other published studies is difficult due to the lack of homogeneity of the classifications used. Generally, RA is the most common class according to FAB classification [19]. The predominance of RCMD subtype in our work, with poor prognosis compared to RA and SA and high-risk subtypes (RAEB 1 and 2) would be due to diagnostic delay and lack of access to specialized services [11].

The incidence of MDS varies according to geographical regions. It is 2.3 in the Netherlands, 2.5 in the UK and Germany [9, 12, 20], of 3.3 and 3.4 in the United States according Rollison and Ma respectively [21, 22] and 6.1 in Lower Normandy [17] (Table II). The lack of objectivity of the diagnostic criteria, the frequent changes in classifications and lack of uniformity in the registration of cases are the causes of variability of the incidence of MDS from one study to another [11, 23]. A national register is essential now to assess the real importance of MDS in our country and to compare the impact and prevalence of this pathology among different regions.

CONCLUSION

The epidemiology of MDS, a subject of great interest at present, is still unknown in our country and in the countries of the region, despite better diagnosis especially through to improved classification criteria and knowledge this entity by cytologists. We observed a marked increase in the frequency of MDS over the years. The age of diagnosis was younger compared to European and North American countries. A national multicenter study involving a larger sample will collect more data for better statistical representation of the epidemiology of MDS in our country, pending the development of a national cancer registry.

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