$-\alpha^{4.2}$ and $--^{SEA}$ carrier status of patients.

Among the 67 Iranian subjects analyzed, α-globin gene mutations were identified in a total of 43 cases (64.2%). The most common α-thal genotypes were the heterozygous ($-\alpha^{3.7}/\alpha\alpha$) and the homozygous ($-\alpha^{3.7}/-\alpha^{3.7}$) forms of the common single gene deletion $-\alpha^{3.7}$, which were observed in 23 (34.3%) and 9 (13.4%) subjects, respectively. Furthermore, 3 subjects (4.5%) were $--^{MED}/\alpha\alpha$, and 2 subjects (3.0%) were $-\alpha^{3.7}/-\alpha^{4.2}$. One individual each (1.5%) was found positive for $-\alpha^{3.7}/--^{MED}$, $-\alpha^{4.2}/--^{MED}$, $\alpha^{4.2}/\alpha\alpha$, $-(\alpha)^{20.5}/\alpha\alpha$, $\alpha^{CS}\alpha/\alpha^{CS}\alpha$, and $\alpha^{CS}\alpha/\alpha\alpha$. In 24 individuals (35.8%) none of the twelve deletions or point mutations analyzed was detected (Table 1). Calculated allele frequencies among our cohort of patients were 32.8% for the $-\alpha^{3.7}$ deletion, 3.7% for the $--^{MED}$ deletion, 3.0% for the $-\alpha^{4.2}$ deletion, 2.2% for Hb Constant Spring (α^{CS}), and 0.7% for the $-(\alpha)^{20.5}$ deletion.

α-thal is not as prevalent as β-thal in Iran, but a significant number of cases with reduced MCV and MCH, normal Hb electrophoresis and normal iron status, are being referred to molecular biology clinics throughout the country as suspected cases of α-thal or normal HbA_2 β-thal. During earlier studies by our group, a high prevalence of the $-\alpha^{3.7}$ single gene deletion among such patients was noted.[10] In agreement with these preliminary data, our present study confirms that $-\alpha^{3.7}$ is by far the most common cause of microcytic, hypochromic anemia in Iran. In addition, we observed other α-globin deletions and point mutations in considerably lower frequencies. We will now use DNS sequencing to investigate the patients without known mutations for possibly abnormal hemoglobins.

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Incidence and characteristics of myelodysplastic syndromes in Ourense (Spain) between 1994-1998

The very few reference epidemiological studies on myelodysplastic syndromes (MDS) have been carried out in Europe: Germany, France, UK and Sweden. We present the first Spanish study on the incidence and characteristics of MDS. The incidence rates, distribution by FAB subtypes, sex and age groups are within the ranges established by the reference studies with minimal differences which we point out and attempt to explain.

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The province of Ourense is located in the southeast of Galicia, Spain. It has 346,913 inhabitants, according to the 1996 Renovation Census.[1] These inhabitants form a stable population with minimal migratory movements. Twenty-eight percent of the population are 65 years of age or older. Around 60% of the province's population lives in a rural environment.[2] There are no nuclear plants nor oil refineries in this region. The province's hospital assistance is distributed between three centers: the Complexo Hospitalario de Ourense (CHOU), the Hospital Comarcal de Valdeorras and the Fundación Hospital Verín, the only provincial centers in which diagnosis and follow-up of MDS patients are carried out. The source for identifying the cases was the bone marrow databases at these hospitals. The sample consists of all the patients diagnosed with MDS according to the FAB classification criteria[3] from January 1, 1994 up to December 31, 1998.

During the study period, 140 new cases of MDS were diagnosed. The crude incidence rate was 8.07/100,000/year (9.11 in men and 7.1 in women). The age standardized incidence rates were: 0 for age <50, 4.4 for age 50-59, 6.8 for age 60-69, 25.5 for age 70-79 and 56.7 for age >79. The incidence and the sex ratio increased with age; therefore, in the ≥ 70 year old age group, the incidence in men is 48.1/100,000/year, whereas in women it is 29.4/100,000/year (Table 1). The mean age at diagnosis was 77.5 years (CI 95%: 75.9, 79.0) with no significant differences between sexes (men 76.9 years and women 78.1 years, p=0.45) nor between FAB subtypes. Eighty-

Table 1. Incidence rates of MDS in Ourense by age and sex.

Age	*Men*	*Women*	*Total*
< 50 yr	0	0	0
50-69 yr	16 / 7.42	10 / 4.20	26 / 5.73
≥ 70 yr	60 / 48.1	54 / 29.4	114 / 36.96
All ages	76 / 9.11	64 / 7.1	140 / 8.07

Number of new cases diagnosed between 1994-1998 and incidence rate (per 100,000 inhabitants per year) according to the 1996 Renovation Census.

nine percent of the cases were 65 years or older and 78% were over the age of 70. The sex ratio was 1.19 (76 men/64 women), with no differences between FAB subtypes (χ^2 0.698, p= 0.952). The distribution of cases according to the FAB subtype has remained stable throughout the period studied. The diagnosis was refractory anemia (RA) in 40 (29%), RA with ringed sideroblasts (RARS) in 43 (31%), RA with excess blasts (RAEB) in 27 (19%), RAEB in transformation in 7 (5%) and chronic myelomonocytic leukemia (CMML) in 23 (16%). Sixty-nine percent of cases came from a rural environment and 31% from an urban environment, which reflects the population structure in the province. In the above mentioned period, there were no cases of spontaneous recovery. Family cases were not diagnosed. There were no therapy-related MDS cases though some occurred afterwards.

Table 2 shows the crude and age-specific incidence rates of the published studies in reference to well-defined populations[4-9] and the present study. The MDS incidence in this population (8.07/100,000/year) is intermediate between that described in the Pays Basque[9] (7.7/100,000/year) and Somerset[7] (9.3/100,000/year). As in all the other studies, we observed a progressive increase in incidence as age increased until the incidence 56.7/100,000/year in the group of people over the age of 70. Unlike other studies in which incidence in people under the age of 50 oscillated between 0.2[4] and 0.7/100,000/year,[5] in our population we do not have any cases in young patients. Given the low incidence of MDS, it is possible that a longer study period may be necessary to pick up cases in younger people. The mean age at diagnosis of our patients (77.5 year) was similar to that published in the other studies,[4,5,8,9] with an elevated percentage in those older than 65 years of age (89%). It was noted that the diagnosis was higher in women than in men,[5,8] but in our series the differences were not statistically significant. We did not observe significant differences in the mean age at diagnosis between the FAB subtypes.

The distribution of cases according to FAB subtypes was similar to that in the other described populations, with a predominance of RA and RARS with respect to the other subtypes. Different from the studies of Radlund *et al.*[5] and Maynadié *et al.*[8] which reported a greater prevalence in men over all in a FAB subtype, such as CMML, in Ourense, as in Dusseldorf[4] and the Pays Basque,[9] we did not observe statistically significant differences between the distinct subtypes, and the sex ratio was close to 1. However, the incidence was greater in men than in women and the disease was more predominant in the elderly. This coincides with what was observed in the three studies that calculated incidence by age and sex.[4,5,8] One proposed hypothesis to explain this fact is the greater exposure of the men to toxic environmental factors in relation to their occupation.[4,5]

We were unable to establish a causal relationship with toxic environmental exposure, a difficulty also encountered in other published works.[4,6,9] None of the patients in our study had received previous chemotherapy or radiotherapy so all the cases were considered as being primary MDS. This differs with the findings in other works which described a percentage of secondary MDS which oscillated between 5.3%[4] and 12.5%.[5] In summary, MDS are characteristically diseases of the elderly population. Given the demographic projection of Spanish and western populations, with a clear tendency to aging, MDS are some of the most frequent hematologic pathologies, and thus it is relevant and interesting to study them. There are no

Table 2. Crude and age-specific incidences of MDS (per 100,000 inhabitants/year).

Authors	*Aul C*[4]	*Radlund*[5]	*Williamson*[6]	*Phillips*[7]	*Maynadié*[8]	*Bauduer*[9]	*Present study*
Geographic area	Düsseldorf (Germany)	Jönköping (Sweden)	Bournemouth (England)	Somerset (England)	Côte d´Or (France)	Pays Basque (France)	Ourense (Spain)
Population	575000	310000	214500	413500	493931	290000	346913
Period	1986-90 *1	1988-92 *2	1981-90	1985-93	1980-90	1993-96	1994-98
Age							
< 50 yr	0.2	0.7	0.5	0.5			0
50-59 yr	4.9	1.6	5.3	2.3	*3	*4	4.45
60-69 yr			15.0	13.9			6.8
70-79 yr	22.8	15	49.0	37.2			25.5
>79 yr			89.0	81.3			56.7
All ages	4.1	3.5	12.6	9.3	3.2	7.7	8.07

**1The studied period was 1975-90, this table only shows the last period (1986-90); *2The studied period was 1978-92, this table only shows the last period (1988-92); *3The age-specific incidence rates by sex , presented in the figures, do not reflect numerical data; *4Only the incidence rate in > 65-year old is indicated: 31.4/100000 /year.*

epidemiological studies in our country and there are few in the world. After comparing our results with those of other European studies, we found only minimal differences between our incidence rates, distribution by FAB subtypes, sex and age groups and those reported in other reference studies.

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Key words: myelodysplastic syndromes, epidemiology, incidence, elderly.

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Safety and efficacy of stem cell mobilization under imatinib therapy

In order to investigate the safety and efficacy of stem cell mobilization in chronic myeloid leukemia patients under imatinib therapy we treated 10 such patients with granulocyte colony-stimulating factor. We observed that none of the patients developed progressive disease under this treatment. Instead, sufficient CD34+ apheresis could be performed in 7 patients and, as assessed by nested reverse transcriptase polymerase chain reaction (RT-PCR), bcr/abl-negative stem cell products could be generated in 3 patients. Interestingly, in 3 other patients with bcr/abl-positivity in 1st round RT-PCR of peripheral leukocytes, bcr/abl transcripts in stem cell products could only be detected by nested RT-PCR.

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Despite encouraging results from clinical trials using imatinib mesylate in patients with chronic myeloid leukemia (CML), some of these patients do not achieve complete cytogenetic remission and/or develop relapsing disease after an initial response. Thus, the emerging problem is how CML patients should be counselled concerning stem cell transplantation (SCT) in the imatinib era.[1] In this context the question frequently raised is whether autologous SCT is a favorable option in this population and whether pre-treatment with imatinib may influence its outcome. This topic is currently widely discussed and it is speculated that autografting in combination with imatinib therapy may provide substantial progress in CML treatment.[2] We support the suggestion of re-evaluating the place of autologous SCT, especially in patients who are not candidates for allografts, and of investigating the efficacy of *in vitro* or *in vivo* purging with imatinib. Such an approach may not only be an important therapeutic alternative in individuals who become refractory to imatinib but could also be of relevance in patients with persisting/resting CML clones despite cytogenetic remission.[3]

To assess the safety and efficacy of stem cell mobilization (SCM) under imatinib therapy we stimulated 10 patients with 10 μg/kg body weight (b.w.) granulocyte colony-stimulating factor (G-CSF) and continued imatinib medication. Written informed consent was obtained from all patients. Three patients were in accelerated phase and received 600 mg imatinib while seven were in chronic phase and received 400 mg imatinib daily. The median duration of CML was 33 months (range: 8–91) and the median duration of imatinib therapy was 15.5 months (range: 6–22). All patients were previously pretreated with interferon-α and developed subsequent intolerance or resistance to this drug. In all patients complete cytogenetic remission was confirmed at least twice by cytogenetic or fluorescent *in situ* hybridization (FISH) analysis before SCM. None of our patients progressed with CML after stimulation with G-CSF (median observation time 18 months). Three patients had sufficient numbers of circulating $CD34^+$ cells (>5/μL) but apheresis did not generate appropriate harvests. Leukapheresis yielding at least a total of 2.0×10^6/kg b.w. $CD34^+$ cells was successful in 7 patients. In 6 of these patients repeated separations[2-4] were needed. In patients with successful SCM the median concentration of $CD34^+$ cells was 3.05×10^6/kg b.w. (range: $2.0\text{-}4.6\times10^6$/kg b.w.). Subsequently, bcr/abl transcripts were detected by nested RT-PCR[4] both in the stem cell preparations (SCP) as well as in peripheral blood leukocytes which were collected within the 2 days before stem cell apheresis.

In two out of three patients who were bcr/abl-negative in peripheral blood samples bcr/abl-negative SCP could be