

LETTER to the EDITOR

**Does Indian Myelodysplastic Syndrome have a Biology Different from that in the West ?**

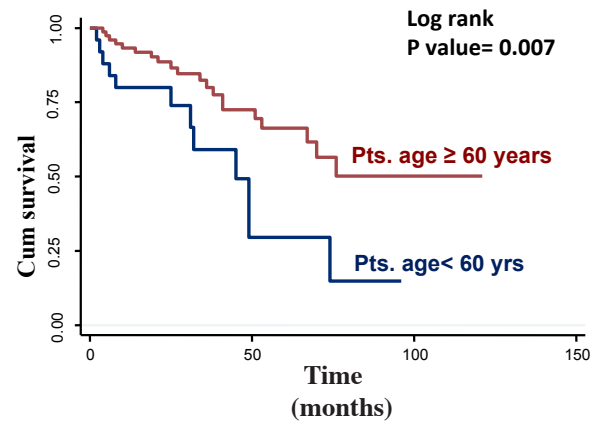
*Asian Pac J Cancer Prev*, 17 (4), 2341-2342

**Dear Editor**

We read with great interest the paper published by Magalhaes et al (2013) about age and gender related disparities in myelodysplastic syndrome (MDS) in the Brazilian population where the older age and female population were more affected. The median age at diagnosis was 67 years (range 15-88 years). Previous studies on MDS indicated that Indian patients may have a different biology from West (Chaubey et al., 2015).

We conducted a study on 100 unselected adult patients with MDS at AIIMS, New Delhi, a Indian tertiary center, from July 2006 through November 2012. Diagnosis of MDS was based on bone marrow aspirate, biopsy, blood cell morphology and cytogenetics whenever available. All these patients were given supportive care with red cell transfusion, platelet transfusion, vitamin B12, folic acid, pyridoxine and vitamin E and treated with cyclosporine and thalidomide whenever possible. The median follow-up time of all the patients was 32 months (range, 5-121 months). The median age at diagnosis was 48 years (range 09-84 years) and 67 of primary MDS patients (67%) were male. 75% of cases had age less than 60 years. This was lower than presenting age in Western reports of 76 years in United States (Ma et al., 2007), 73 years in Dusseldorf, Germany (Neukirchen et al., 2011) and 70 years in Spain

(Sole et al., 2005). In Asia MDS has been reported to occur more frequently in younger individuals (Japan (57 years), Korea (53 years) and China (59 years) (Lee et al., 1999; Chen B et al., 2005; Matsuda et al., 2005). The reason for the high incidence in younger individuals is still unclear, and the differences in disease features between young and elderly patients with MDS have been not well recognized. In our study male patients were older (median age 55.5 years) than female group (median age 43 years). This is similar to Brazilian study (Silvia et al., 2013) but sharply



**Figure 1. Kaplan–Meier curve** shows the overall survival (4 years) of patients according to age.

**Table 1. Comparison of Cytogenetics Risk Groups and WHO subtypes according to age groups.**

| WHO subtypes<br>(n=51) | Good cytogenetics<br>(n=34) |             |        | Intermediate + poor cytogenetics (n=17) |                 |        |
|------------------------|-----------------------------|-------------|--------|---|-----------------|--------|
|                        | Age <60 yrs (%)             | Age ≥60 yrs | Total  | Age <60 yrs (%)                         | Age ≥60 yrs (%) | Total  |
|                        | (n=26)                      | (n=8) (%)   | (n=34) | (n=9)                                   | (n=8)           | (n=17) |
| RCUD                   | 13 (50)                     | 2 (25)      | 15     | 0                                       | 2 (25)          | 2      |
| RARS                   | 1 (3.8)                     | 2(25)       | 3      | 0                                       | 1(12.5)         | 1      |
| RCMD                   | 4 (15.3)                    | 1 (12.5)    | 5      | 2                                       | 1(12.5)         | 3      |
| Deletion 5q            | 4 (15.3)                    | 2 (25)      | 6      | 0                                       | 0               | 0      |
| MDS-U                  | 0                           | 0           | 0      | 0                                       | 1 (12.5)        | 1      |
| RAEB-1                 | 1 (3.8)                     | 0           | 1      | 2 (22.2)                                | 3 (37.5)        | 5      |
| RAEB-2                 | 3 (11.5)                    | 1(12.5)     | 4      | 5 (55.5)                                | 0               | 5      |
| IPSS Score             |                             |             |        |   |                 |        |
| Low                    | 20                          | 5           |        | 0                                       | 0               |        |
| Intermediate           | 6                           | 2           | 0.3    | 5                                       | 6               | 0.6    |
| High                   | 0                           | 1           |        | 4                                       | 2               |        |
| Transfusion dependency | 23 (88)                     | 6 (75)      | 0.5    | 8 (89)                                  | 6 (75)          | 0.5    |
| Disease Progression    | 3 (12)                      | 1 (12)      | 1      | 5(56)                                   | 0(0)            | 0.02   |

\*Fisher Exact/ Chi Square Test Applied

different from that reported by Neukirchen et al. (2011).

The distribution of MDS subtypes was as follows : refractory anemia unilineage dysplasia (RCUD) (49%) ,refractory anemia with excessive blasts-2 (RAEB-2) (16%), refractory anemia with excessive blasts -1 (RAEB-1) (10%) , refractory cytopenia with multilineage dysplasia (RCMD) (10%), refractory anemia with ringed sideroblasts (RARS) (6%), del (5q) (6%), refractory anemia with excessive blasts 1 – ringed sideroblasts (RAEB1-RS) (1%), refractory cytopenia with multilineage dysplasia –ringed sideroblasts (RCMD-RS) (1%) and MDS unclassified (MDS-U) (1%).

Cytogenetic study was available in 51 patients. Normal karyotype was present in 26 (51%) patients, while abnormal karyotype was present in 25(49%) patients. Thirty four (66.7%) patients had good cytogenetics (normal cytogenetics, del (5q), monosomy 20), 7(13.7%) as having intermediate cytogenetics (deletion 3q, deletion 6q, trisomy 8) and 10 (19.6%) as having poor cytogenetics (monosomy 7 and complex). Monosomy 7 was the most frequent cytogenetic abnormality detected in 7 of 51 (13.7%) patients, followed by deletion 5q - detected in 6 (11.8%) and trisomy 8 and complex karyotype each in 3 (5.9%) patients. Unreported cytogenetic aberrations like, deletion 3q and deletion 6q were seen in one case each. When the cytogenetics was compared in the different WHO subtypes it was found that 55.5% of patients with RAEB2 and age less than 60 years had poor or intermediate cytogenetics as compared to the patients with age  $\geq$ 60 years which suggests that poor cytogenetics was more prevalent in high risk younger patients. Also the disease progression was observed only in the patients with age <60 years and poor cytogenetics progressed and no progression was observed in the patients having age  $\geq$ 60 years and poor cytogenetics ( $p < 0.02$ ). (Table 1). Out of 100 patients studied twenty one patients progressed during the follow up. Two patients progressed from RA to AML 2 patients with RA to RCMD (4/49; 8.1%), 10 patients from RAEB2 to AML, 1 patient with RAEB-2 to ALL and 1 patient with RAEB2 with del (5q) to MF. (12/16; 75%), 5 patients with RAEB-1 to AML (5/11; 45%). The median time of progression was 15 months (Range 1-16 months) in these patients.

Strikingly, none of the patient with age  $\geq$ 60 years with poor or intermediate cytogenetics progressed during the course of the study. There was no difference found when the clinical and haematological parameters were compared with good and poor cytogenetics in two age groups. Out of 100 patients studied 32 patients died during the follow up. The median follow-up time of all the patients was 32 months (range, 5-121 months).

The most important finding of this study was that the patients with age <60 years had significantly low median overall survival (4 years) as compared to the group of patients with age  $\geq$ 60 years (45 months vs. - months (not reached);  $p = 0.007$ ). The survival probability of patients with age  $\geq$ 60 years at 24 and 48 months was 0.88 (95% CI, 0.78-0.94) and 0.72 (95% CI, 0.57-0.82) respectively. (Figure 1) This is in contrast to the literature from the Western and European countries where the patients with age more than 60 years had poor outcome (Goldberg et

al., 2010; Sekeres et al., 2010).

Our findings suggests age related disparities at diagnosis in this well-defined sample of Indian population as well as poorer prognostics features possibly causes poorer survival. In summary, MDS in India is diagnosed at an earlier age than in Western countries. Young patients present with more advanced disease, more poor cytogenetics and significantly shorter survival than older patients. We interpret these data as an indication that the younger patients in India with MDS may have some different biology than reported from the other part of the world. We agree with other studies that large-scale studies and better comprehension of the influence of ethnicity and environment are necessary to understanding the biology of this disease, considered to be one of the most frequent hematological disorders in the fast-growing young age groups especially in India.

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