Molecular Cytogenetics

RESEARCH Open Access

Higher prevalence of poor prognostic markers at a younger age in adult patients with myelodysplastic syndrome – evaluation of a large cohort in India

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Abstract

Background The karyotype is a major determinant of prognosis in myelodysplastic syndrome (MDS). Details of the cytogenetic profile of MDS in South Asia are limited because cytogenetic services are not widely available.

Methods We performed a retrospective analysis of the cytogenetic and clinicopathologic profile of adult primary MDS seen consecutively at a tertiary-care centre in South India between 2003 and 2017. Patients were re-categorised according to the 2022 World Health Organisation (WHO) and the International Consensus classifications (ICC).

Results There were 936 patients aged 18–86 years (median age 53, 65% males), with MDS with del 5q, low blasts and increased blasts in 7.5%, 58.4% and 34.1% respectively. Clonal abnormalities were seen in 55% of patients, with solitary abnormalities in 29.8% and complex karyotypes (CK, ≥ 3 abnormalities) in 15%. The most frequent abnormalities were monosomy 7/deletion 7q (16.1%), deletion 5q (14.5%), trisomy 8 (11.5%), and deletion 20q (5.1%). Cytogenetic prognosis groups were distributed as follows: very good, 2%; good, 55.6%; intermediate, 16.2%; poor, 15%; very poor, 11.2%. Clinical (IPSS-R) risk stratification (842 patients) showed: very low-risk, 3.9%; low-risk, 30.9%; intermediate-risk, 24.2%; high-risk, 21%; very high-risk, 20%. Age-adjustment (IPSS-RA) raised the very low-risk group to 12.4%; the other groups decreased by 1–3% each.

Conclusion The most significant finding of this cytogenetic analysis of MDS in India is that abnormal karyotypes with poor prognosis markers including monosomy 7 and CK were more frequent than in most other reports, among patients who were overall younger. Trisomy 8, deletion 20q, the IPSS-R intermediate-risk and both high-risk groups were more common than in the West. Trisomy 8 was less common than in South-East Asia while CK and deletion 20q were comparable. Evaluation of such large cohorts highlights the unique features of MDS in different parts of the world. These findings suggest that there could be differences in predisposing factors, environmental or genetic, and emphasise the need for further exploration to better understand the varied nature of MDS.

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Keywords Myelodysplastic syndrome, Chromosomal abnormality, Clinical risk groups, Complex karyotype, Cytogenetics, Cytogenetic prognosis groups, Deletion 5q, Monosomy 7, IPSS-R, Trisomy 8

Introduction

The myelodysplastic syndromes (MDS) are a group of bone marrow disorders characterised by at least one peripheral cytopenia and dysplasia of one or more haematopoietic lineages due to ineffective haemopoiesis associated with neoplastic transformation of haematopoietic stem cells [1]. These disorders show considerable variation with respect to the severity of cytopenia and dysplasia, clinical course, including risk of transformation to acute myeloid leukemia (AML), and response to therapy [1]. Cytogenetic abnormalities are seen in about 50% of MDS [2]. The presence of an abnormal karyotype provides evidence that a clonal proliferation underlies the refractory cytopenia being investigated [1, 2].

Earlier classifications of MDS have been revised by the World Health Organisation (WHO) since 2001 to include the subtype MDS with isolated del 5q (MDS-del 5q) which is based on the karyotype [3–7].

The most recent (2022) WHO classification and International Consensus classification (ICC) also describe two subtypes based on the presence of the *SF3B1* mutation and biallelic *TP53* inactivation [8, 9]. These subtypes are termed MDS with low blasts (LB) and *SF3B1* mutation (MDS-*SF3B1*) and MDS with biallelic *TP53* inactivation (MDS-bi*TP53*) by the WHO [8]. The ICC refers to these two subtypes as MDS with mutated *SF3B1* and MDS with mutated *TP53.* [9]. According to the 2022 WHO classification, the presence of ≥15% ring sideroblasts (RS) may substitute for the *SF3B1* mutation and the subtype may also be termed MDS with low blasts and ring sideroblasts [8].

Cytogenetic findings have been used in prognostic scoring systems since 1997 because the chromosomal complement of the marrow is a major determinant of prognosis and response to therapy [1, 2, 10–12]. In the most frequently used Revised International Prognostic Scoring System (IPSS-R), the karyotype has the widest range of prognostic score values, emphasising its importance in determining the clinical risk score [12]. Although the risk-stratification of MDS is refined further by the use of the more recently described IPSS-Molecular (IPSS-M) which combines the mutational profile with haematological and cytogenetic parameters, it is likely that the IPSS-R will continue to be in use until advanced molecular testing is more widely available [13].

Analyses of cytogenetic findings in MDS from different parts of the world vary with respect to the classification systems used, modes of ascertainment of abnormalities and the numbers and subtypes of patients analysed [14–28]. Reports from India are relatively few, and except for two, describe small numbers of patients [29, 30]. We describe the karyotypes associated with primary MDS and their associated clinicopathological features in a large series of adult patients seen at a referral hospital in South India.

Patients and methods

Patient cohort

The study group consisted of all adults with primary MDS seen consecutively in the Department of Haematology, Christian Medical College (CMC), Vellore, India between 2003 and 2017, and who underwent conventional cytogenetic analysis (CCA). The diagnosis of MDS was based on a combination of clinical examination, blood and bone marrow findings and cytogenetic analysis as well as the absence of specific antecedent medical conditions.

Molecular genetic studies were not performed during the period of this study. Patients who had received chemotherapy and/or radiotherapy for an antecedent haematological or other neoplasm or had other causes of cytopenia including those associated with hypoplastic or cellular marrows with no dysplasia and normal cytogenetics were excluded from the analysis.

Haematological evaluation

All patients underwent complete blood count (CBC) analysis and morphological assessment of bone marrow aspirates and trephine biopsies at diagnosis using Romanowsky-stained slides, cytochemistry and reticulin staining as well as immunohistochemistry, as appropriate. The morphologic diagnosis was based on the WHO classification system in use at the time.

However, to provide contemporary relevance in this report, MDS subtypes were re-categorised according to the ICC and WHO 2022 classifications based on morphological and cytogenetic findings. MDS, unclassifiable (MDS-U) which comprised three sub-categories in the WHO 2016 classification and which has been removed from the WHO 2022 classification was re-categorised to the extent possible. Specifically, the sub-category of MDS-U, "MDS-U with single lineage dysplasia and pancytopenia" was categorised as "MDS with low blasts" while the sub-category "MDS-U with defining cytogenetic abnormality" was excluded from the cases in the WHO 2022 categories, but retained in the ICC 2022 which has termed this subtype "MDS, NOS without dysplasia". We did not have any patients with the third subcategory, MDS-U with 1% blood blasts. MDS with low blasts was sub-categorised as proposed by the WHO

Table 1 Clinical, haematological and cytogenetic features of adult primary myelodysplastic syndrome (MDS)

Table 1A: Clinical and haematological features	
Characteristic	**N (%)**
No. of patients with MDS	988
Median age (range)	53 years (18–86)
No. of patients ≥ 21 years (%)	899 (96)
Median age of patients ≥ 21 years (range)	53 years (21–86)
No. of patients ≥ 40 years (%)	696 (74)
Median age of patients ≥ 40 years (range)	58 years (40–86)
Males / females (M: F ratio)	607/329 (1.8:1)
Blood counts	
Hemoglobin, g/dL, $n=929$	
<10	787(84.7)
≥10	142(15.3)
Platelet count, $\times10^9$/L, $n=929$	
<100,000	619(66.6)
≥100,000	310(33.4)
Absolute neutrophil count (ANC), $\times10^9$/L, $n=919$	
<0.8	610(66.4)
≥0.8	309(33.6)
Single cytopenia	237(25.5)
Anemia	165(17.8)
Thrombocytopenia	51(5.5)
Leucopenia	21(2.3)
Bicytopenia	311(33.5)
Anemia & thrombocytopenia	165(18)
Anemia & leucopenia	98(10.7)
Thrombocytopenia & leucopenia	48(14.1)
Pancytopenia	346(37.6)
Table 1B. Overview of cytogenetic findings	
Characteristic	N (%)
Successful cytogenetic analyses	936 (94.7)
Normal karyotypes	421(44.9)
Clonal cytogenetic abnormalities	515(55)
Numerical abnormalities only	131 (25.4)
Structural abnormalities only	201(39)
Numerical and structural abnormalities	183 (35.5)
Cytogenetic abnormalities	
Single abnormality	279(29.8)
Two abnormalities	70(7.5)
≥2 independent non-complex clones	25(2.7)
Complex KT, ≥3 abnormalities	141(15)
Complex KT with 3 abnormalities	36(3.8)
Complex KT with >3 abnormalities	105(11.2)
Table 1C. Cytogenetic prognosis and clinical risk groups	
Cytogenetic prognosis groups (as per CCSS and IPSS-R)	N (%)
Very good prognosis	19(2)
Good prognosis, all / abnormal KT only	520(55.6)/99(10.6)
Intermediate prognosis	152(16.2)
Poor prognosis	140(15)
Very poor prognosis	105(11.2)
Clinical (IPSS-R) risk groups, $n=842$	N (%)
Very low risk	33(3.9)
Low risk	260(30.9)
Intermediate risk	204(24.2)

Table 1 (continued)

High risk	177(21)
Very high risk	168(20)

Blood counts categorised as per IPSS-R; KT, karyotype; CCSS, comprehensive cytogenetic scoring system used in IPSS-R (Schanz et al. [15]); IPSS-R, Revised International Prognostic Scoring System (Greenberg et al. [12])

2022. Clinical risk scores (IPSS-R) were calculated as per available data, and adjusted for age (IPSS-RA) [12].

Cytogenetic analysis

Conventional cytogenetic analysis (CCA) was performed on all patients using standard protocols; FISH analysis using locus-specific probes for chromosomes 5, 7 and 20 was done for confirmation of suspected abnormalities [31, 32]. It is not our routine practice to use FISH panels for the work-up of patients with MDS. Karyotypes with <15 metaphases were excluded unless a clonal abnormality was present. Karyotypes were categorised into prognostic groups according to the IPSS-R categories which are based on the comprehensive cytogenetic scoring system (CCSS) described by Schanz et al. [12, 15]. Complex karyotypes with 3 or >3 abnormalities were classified separately based on their prognostic significance according to the IPSS-R.

Data collection and analysis

We performed a retrospective analysis of the cytogenetic and clinicopathologic profile of these patients. These data were extracted from the computerised hospital information system and laboratory databases that are carefully maintained for each patient as standard practice in our institution.

We also compared our findings with studies from the West (Europe, including Austria, Germany, Italy, Spain, Sweden and U.S.A), South-East (S.E) Asia (Japan, China, South Korea and Taiwan), South (S.) Asia (India and Pakistan) and Africa (Tunisia) which had at least 100 patients and did not include those with translocations which are now considered to be definitive for AML [14–23, 25, 28–30, 33–35]. Some of these studies used the French-American-British (FAB) classification and therefore included chronic myelomonocytic leukemia (CMML) and refractory anemia with excess blasts in transformation (RAEB-t) which were categorised as MDS at the time, as well as AML following MDS or myelodysplastic/myeloproliferative neoplasms (MDS/MPN) and/or secondary MDS [14–16, 18]. Weighted averages were used to compare frequencies in each region (upto 13,428 patients from the West, 2713 from South-East Asia and 190–347 from S.Asia and Tunisia). The study was approved by the Institutional Review Board of CMC, Vellore.

Statistical analysis

Data were analysed using SPSS Statistics version 21.0 (IBM Corp) and SAS software, version 9.4 (SAS Institute). Descriptive measures such as median and range were presented for continuous variables. For categorical variables, counts and proportions were presented. Categorical variables were compared using the Chi-square test, unless the expected number of subjects in any one category was less than five, in which case Fisher's exact test was used. The Mann Whitney-U test was used for comparing two independent groups, while the Kruskal-Wallis test was used for the comparisons involving more than two groups. All statistical tests were two-sided, and a $p<0.05$ level was considered as statistically significant.

Results

Patients

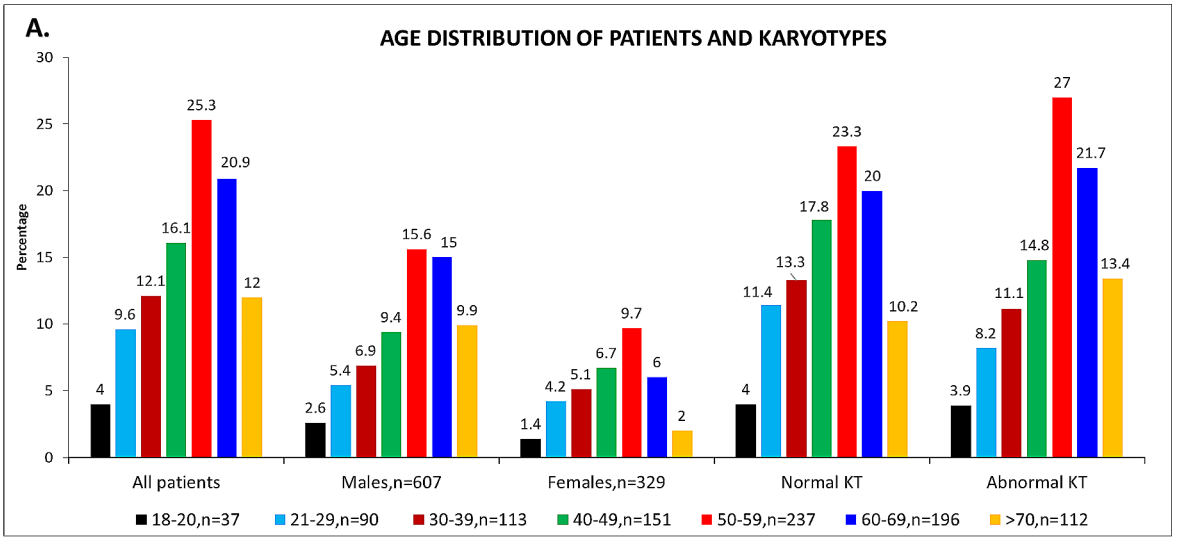
A total of 988 patients were diagnosed to have primary MDS during the period of this study. Adequate karyotypic data was available for 936 (94.7%) of them who were included for further analysis in this study.

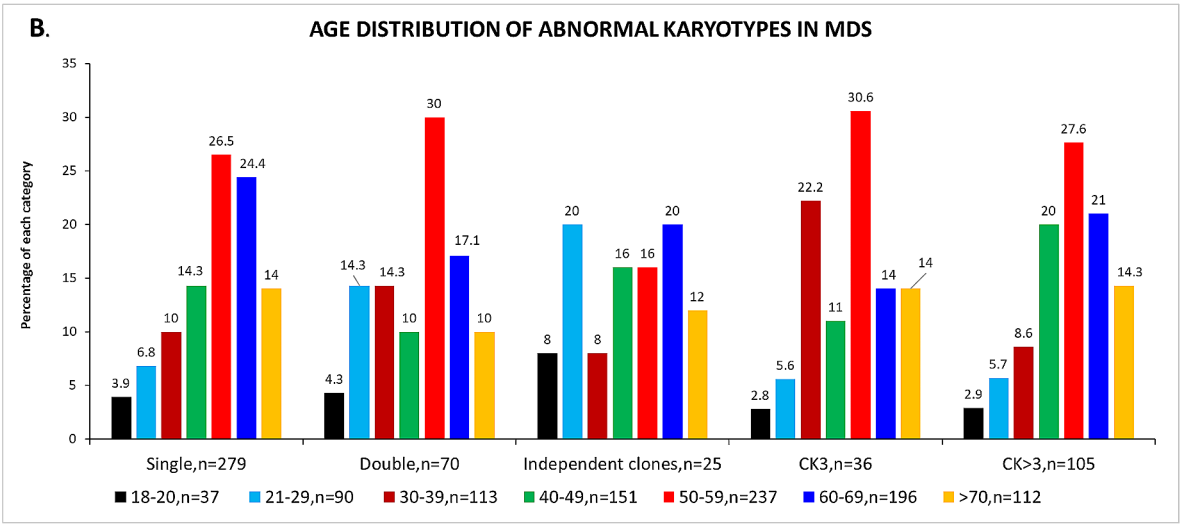
The median age of the study cohort was 53 years (range 18–86). There were 607 (65%) males and 329 females (35%). Clonal cytogenetic abnormalities were seen in 515 (55%) patients, and normal karyotypes in 421 patients (45%) (Table 1).

Overview of age and sex distribution and cytogenetic subgroups. (Fig. 1; Table 2 & Additional File 1)

The number of patients progressively increased from the second decade (4%) to the sixth decade (25%) and declined subsequently (60–69 years, 21% and ≥70 years, 12%) (Fig. 1A). A spike in the sixth decade (23–31%) was noted in all categories of abnormal karyotypes except those with independent non-complex clones (IncC, $n=25$) which were most common (20% each) in the third and seventh decades (Fig. 1B, C).

Complex karyotypes (CK) with ≥3 abnormalities were seen in 15% of patients and abnormalities associated with a poor and very poor prognosis (unfavourable karyotypes) were seen in 26.2% of patients (27.4% and 47.6% of abnormal karyotypes, respectively). The clinical, haematological and cytogenetic features of these patients are shown in Tables 1 and 2 and Fig. 1, and details of the MDS subtypes as per the 2022 WHO and ICC classifications are shown in Additional File 1.





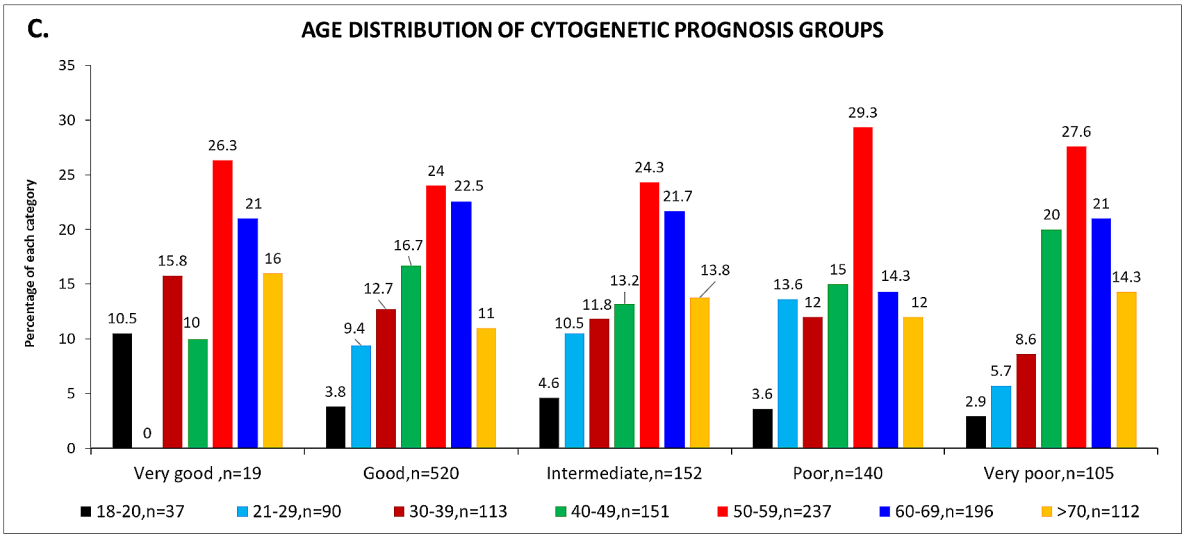


Fig. 1 Age distribution of patients, normal and abnormal karyotypes and cytogenetic prognosis groups

Table 2 Clinical and haematological features of cytogenetic subgroups and MDS subtypes

Table 2A: MDS subtypes and cytogenetic subgroups – correlation with clinical and haematological features

Characteristic	Number (%)	Age, Median (Range)	Males, *n* (%)	Females, *n* (%)	Hb[a], g/dL Median (range)	Plt[b], ×10[9]/L Median (range)	ANC[c], ×10[9]/L Median (range)
MDS subtypes							
ICC and WHO 2022,n = 70							
MDS with (isolated) del 5q	70(7.5)	57(19–82)	26(37.1)	44(62.8)	6.5(2.1–12.5)	179.5(6–794)	2.1(0.01–37.9)
ICC 2022,n = 866							
MDS, not otherwise specified (NOS)	547(58.4)	52(18–86)	369(67.4)	178(32.5)	7.8(2.4–16)	47(2–750)	1.5(0.01–38.5)
MDS with excess blasts (EB)	319(34.1)	53(18–82)	212(66.4)	107(33.5)	7.8(2–14)	37(2–656)	1.1(0.01–28.4)
WHO 2022,n = 849*							
MDS with low blasts (LB)	530(57.7)	52(18–86)	369(67.4)	178(32.5)	7.8(2.4–16)	47(2–750)	1.5(0.01–38.5)
MDS with increased blasts (IB)	319(34.7)	53(18–82)	212(66.4)	107(33.5)	7.8(2–14)	37(2–656)	1.1(0.01–28.4)
Patients with complete blood counts,n = 919							
Pancytopenia absent	573 (62.4)	54 (18–86)	366(63.9)	207(36.1)	8.1(2.1–16)	107(2-794)	2.4 (0.01–38.5)
Pancytopenia present	346 (37.7)	51.5 (18–82)	228(65.8)	118(34.1)	7.3(2–9.9)	22(2–98)	0.5(0.01–1.8)
Details of normal and abnormal karyotypes (KT),n = 936							
All KT	936(100)	53(18–86)	607(65%)	329(35%)	7.7(2–16)	45(1.1–794)	1.49(0.01–38.5)
Normal KT	421 (45)	51(18–84)	273(64.8)	148(35.1)	7.8 (2.4–15)	63.5(2–750)	1.8 (0.01–38.5)
Abnormal KT	515 (55)	54(18–86)	334(64.8)	181(35.1)	7.7 (2–16)	40 (2–794)	1.2 (0.01–37.9)
Karyotypes in pancytopenia,n = 346							
Normal KT	130 (37.6)	46.5(18–80)	81(62.3)	49(37.7)	7.3 (2.7–9.9)	22.5 (4–98)	0.6 (0.01–1.8)
Abnormal KT	216 (62.4)	52(18–82)	147(68.1)	69(31.9)	7.3 (2-9.9)	21.5 (2–96)	0.44 (0.01–1.8)
Number of cytogenetic abnormalities in 515 abnormal karyotypes, n (% of all karyotypes)							
Single abnormality	279(29.8)	55(18–86)	187(67)	92(33)	7.7(2–13.3)	56(2–794)	1.5(0–37.9)
Double abnormality ^^	70(7.5)	52.5(18–81)	50(71.4)	20(28.6)	7.9(2.5–16)	35(3–581)	1.1(0–8)
≥ 2 independent non-complex clones	25(2.7)	49(18–78)	18(72)	7(28)	8(4.8–10.2)	31(7–252)	0.6(0.1–3.7)
Complex KT with 3 abnormalities	36(3.8)	52.5(20–77)	18(50)	18(50)	7.4(4–12.1)	26(2–656)	1(0–6.8)
Complex KT with > 3 abnormalities	105(11.2)	52.5(18–81)	61(58.1)	44(41.9)	7.7(2.8–14.2)	27.5(5–636)	0.6(0–27)

Table 2B: MDS cytogenetic prognosis groups – correlation with clinical and haematological features.

Characteristic	Number (%)	Age, Median (range)	Males, n (%)	Females, n (%)	Hb[a], g/dL Median (range)	Plt[b], ×10[9]/L Median (range)	ANC[c], ×10[9]/L Median (range)
Distribution of cytogenetic prognosis groups (as per CCSS used in IPSS-R),n = 936							
Very good prognosis	19(2)	53(20–77)	18(3)	1(0.3)	7.1(2.7–11.8)	30(4–231)	0.8(0–21.2)
Good prognosis, all / abnormal KT only	520(55.6)/99(10.6)	53(18–84)	321(52.9)	199(60.5)	7.6(2.1–15)	73(2–794)	1.9(0–38.5)
Intermediate prognosis	152(16.2)	53(18–86)	108(17.7)	44(13.4)	8.3(2–16)	48(3–523)	1.2(0–20.9)
Poor prognosis	140(15)	52(18–81)	99(16.3)	41(12.5)	7.7(2.5–13.2)	23.5(2–656)	0.8(0–11)
Very poor prognosis	105(11.2)	55(18–82)	61(10)	44(13.4)	7.7(2.8–14.2)	27.5(5–636)	0.6(0–27)

[a] Hb, haemoglobin; [b] Plt, platelet count; [c] ANC, absolute neutrophil count; *, without 17 MDS-NOS without dysplasia; ^^, with del 5q, ***n*** = 16 including one with minus 7; minus 7, ***n*** = 18 including the one with del 5q; minus 5, del 7q, ***n*** = 1 each; other, ***n*** = 35; CCSS, comprehensive cytogenetic scoring system used in IPSS-R (Schanz et al. [15]); IPSS-R, Revised International Prognostic Scoring System (Greenberg et al. [12])

Frequently seen abnormalities and cytogenetic prognosis groups (Table 3, Figs. 2, 3, 4 and 5 & Additional File 2)

Our most common abnormality was monosomy (minus) 7/ del 7q (7q-) in 151(16.1%) patients, and 159(17%), if der(1;7)(q10;p10) was included (29.3% and 30.9% of abnormal karyotypes respectively).

The del 5q (14.5%) and trisomy (plus) 8 (11.5%) were our next most common abnormalities (26.4% and 21% of abnormal karyotypes respectively). The del 5q was

Table 3 Age & sex distribution of recurrent cytogenetic abnormalities in MDS

Abnormality	*N* (%)	Sex		Age, median	Age, years, *n* (%)						
		M	F	(range)	18–20	21–29	30–39	40–49	50–59	60–69	>70
Chr 1 abn	50(5.3)	31	19	43(18–73)	4(8)	3(6)	13(26)	5(10)	10(20)	12(24)	3(6)
der (1;7)	8(0.9)	6	2	47(26–60)	0(0)	1(12.5)	1(12.5)	2(25)	3(37.5)	1(12.5)	0(0)
t(3;3)	9(1)	5	4	46(27–58)	0(0)	2(22.2)	0(0)	3(33.3)	0(0)	4(44.4)	0(0)
−5	30(3.2)	19	11	51(18–72)	1(4)	4(9.5)	5(11.9)	7(15.9)	7(25.4)	5(21.1)	1(12.3)
5q	136(14.5)	67	69	53(19–82)	2(1.5)	4(2.9)	14(10.3)	21(15.4)	35(25.7)	41(30.1)	19(14)
t(6;9)	4(0.3)	1	2	37(25–47)	0(0)	2(50)	0(0)	1(25)	0(0)	0(0)	1(25)
−7	123(13.1)	82	41	53(18–81)	4(4.1)	15(9.2)	12(12.4)	19(16.2)	36(24.7)	18(21.9)	19(11.4)
7q−	28(3)	16	12	53(19–86)	3(3.7)	2(9.7)	4(12)	3(16.3)	8(25.2)	6(20.9)	2(12.1)
+8	108(11.5)	74	34	53(19–85)	2(4.2)	11(9.5)	10(12.4)	16(16.3)	32(24.8)	20(21.3)	17(11.5)
9q−	16(1.7)	11	5	52(22–73)	0(0)	2(12.5)	2(12.5)	3(18.8)	3(18.8)	5(31.3)	1(6.3)
11q−	19(2)	12	7	57.5(39–82)	0(0)	0(0)	1(5.3)	1(5.3)	7(36.8)	6(31.6)	4(21.1)
−11	11(1.2)	6	5	56.5(40–74)	0(0)	0(0)	0(0)	4(36.4)	2(18.2)	4(36.4)	1(9.1)
12p*	15(1.6)	10	5	59(45–82)	0(0)	0(0)	0(0)	1(6.7)	6(40)	6(40)	2(13.3)
−13	17(1.8)	10	7	52(18–75)	1(5.9)	0(0)	2(11.8)	2(11.8)	4(23.5)	6(35.3)	2(11.8)
13q−	11(1.2)	7	4	52(21–71)	1(9.1)	1(9.1)	0(0)	3(27.3)	1(9.1)	3(27.3)	2(18.2)
−17	28(3)	16	12	53(18–81)	2(7.2)	2(7.1)	5(17.9)	2(7.1)	6(21.4)	7(25)	4(14.3)
17p−	5(0.5)	1	4	58(44–76)	0(0)	0(0)	0(0)	2(40)	2(40)	0(0)	1(20)
i(17)q	8(0.9)	6	2	54(25–79)	0(0)	1(12.5)	0(0)	1(12.5)	0(0)	3(37.5)	3(37.5)
t(17)p	3(0.3)	3	0	72(71–73)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	3(100)
−18	28(3)	22	7	58(40–82)	0(0)	2(7.1)	0(0)	7(25)	11(39.3)	6(21.4)	2(7.1)
+19	15(1.6)	9	6	53(27–70)	0(0)	2(13.3)	0(0)	2(13.3)	6(40)	4(26.7)	1(6.7)
20q−	48(5.1)		10	53(20–82)	2(4.2)	1(2.1	1(2.1)	10(20.8)	11(22.9)	13(27.1)	10(20.8)
−20	29(3.1)	16	12	55(27–82)	0(0)	1(3.4)	2(6.9)	6(20.7)	9(31)	7(24.1)	4(13.8)
+21	31(3.3)	19	12	52(22–77)	0(0)	4(12.9)	2(6.5)	2(6.5)	15(48.4)	6(19.4)	2(6.5)
+22	14(1.5)	6	8	55(29–77)	0(0)	1(7.1)	0(0)	1(7.1)	8(57.1)	3(21.4)	1(7.1)
−X	11(1.2)	2	9	55(31–75)	0(0)	0(0)	4(36.4)	1(9.1)	2(18.2)	1(9.1)	3(27.3)
−Y	24(2.6)	24	0	53(20–82)	2(8.3)	0(0)	3(12.5)	5(20.8)	6(25)	3(12.5)	5(20.8)
Other abn	87(9.3)	60	27	53(18–82)	4(4.5)	7(8)	16(18.4)	7(8)	27(31)	18(20.7)	8(9.2)
Mar	98(10.5)	54	44	55(18–82)	4(4.1)	10(10.2)	9(9.2)	13(13.3)	28(28.6)	24(24.5)	10(10.2)
MK	113(12.1)	69	44	54(18–82)	3(2.7)	8(7.1)	11(9.7)	20(17.7)	34(30.1)	21(18.6)	16(14.2)

abn, abnormality/ies; del, deletion; der, derivative; i, isochromosome; mar, marker chromosomes; − (minus), monosomy or loss; + (plus), trisomy; t, translocation; *One t(12)p, male, 54 years, not included; MK, monosomal karyotype

present in 79 non-complex karyotypes, 70 (88.6%) of which could be categorised as MDS-del 5q.

Apart from the del 20q (5.1%), the other MDS-related abnormalities accounted for ≤3.5% each. Monosomal karyotypes were seen in 113 (12.1%) patients, 98 of whom had CK while 15 had two abnormalities. Abnormalities usually seen as part of CKs included monosomies 5,17,18 and 20 (>95%), trisomy 19, minus X (>90%), monosomy 13 and marker chromosomes (>80%). CKs were also seen in 35 of 38 (92%) karyotypes in which monosomy 7 ($n=25$) /del 7q ($n=13$) were associated with monosomy 5/del 5q.

There were 21 patients (2.2%) with "MDS-defining" translocations which comprised the t(3;3)(q21;q26.2) in 0.96% and the t(6;9)(p22;q34), t(1;3)(p36.3;q21.1), t(3;21)(q26.2;q22.1) and t(2;11)(p21;q23) in 0.2–0.4% each. Other recurrent translocations included the t(3;5)(q21;q31), t(4;12)(q12;p13), t(5;11)(q31;q23, t(11;19)(q23;p13.3) and t(20;21)(q13;q22) which were seen in 0.1–0.3% of patients (Additional File 2).

The inv(3)(q21q26.2), the t(11;16)(q23.3;p13.3), and the idic(X)(q13), also termed MDS-defining abnormalities were not seen in this cohort.

Clinical risk scores (Fig. 6)

Data for calculation of clinical risk scores as defined by the Revised International Prognostic Scoring System (IPSS-R) was available in 842 (90%) patients of whom 817 were ≥21 years and 630 were ≥40 years. The distribution of the IPSS-R intermediate-risk and both high-risk groups was similar (20–24%) compared to the low-risk (31%) and very low-risk groups (3.9%); however, when adjusted for age (IPSS-RA), the number of patients in the very low-risk group increased to 12.4% while the other groups decreased by 1–3% each.

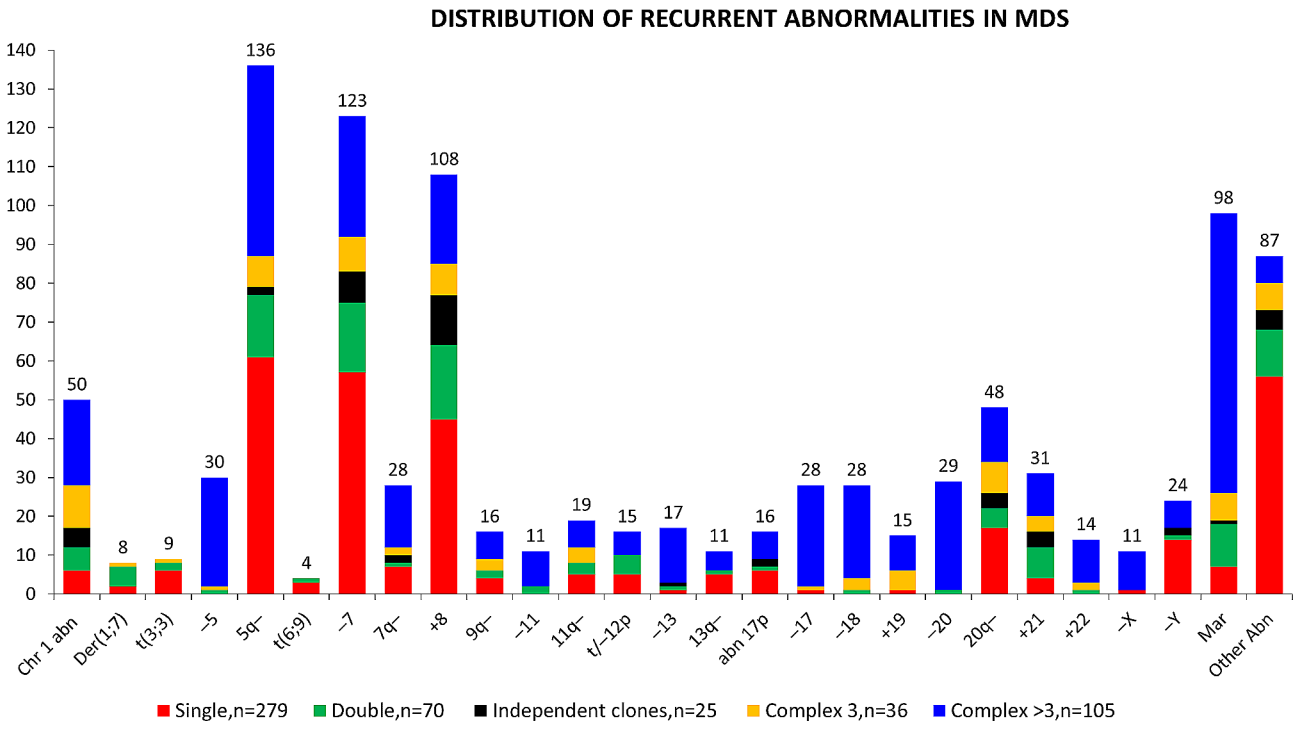


Fig. 2 Distribution of recurrent abnormalities in MDS

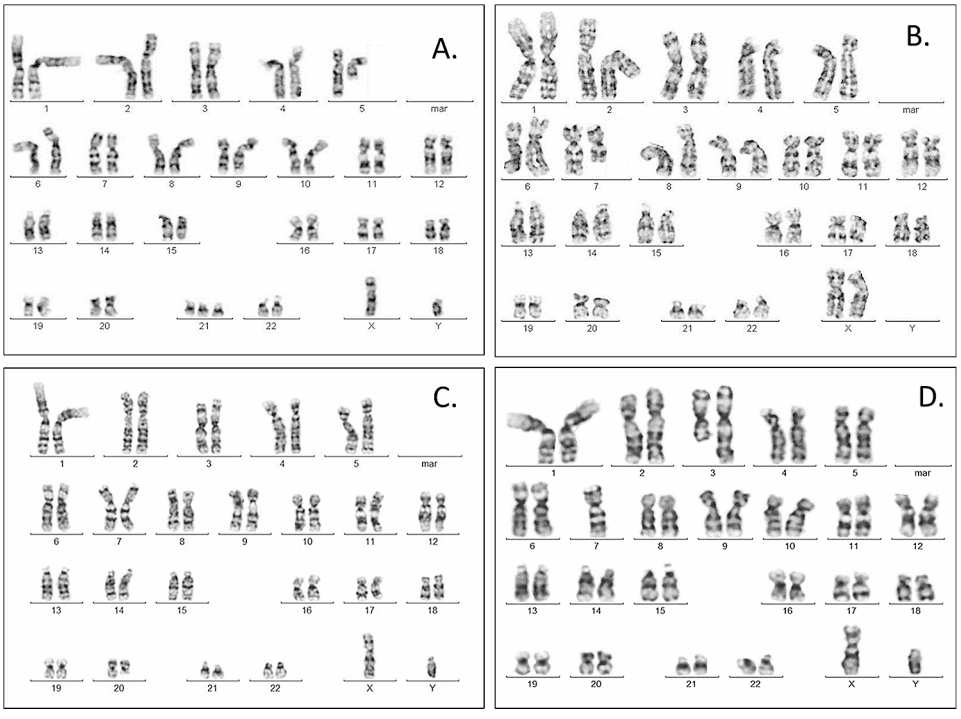
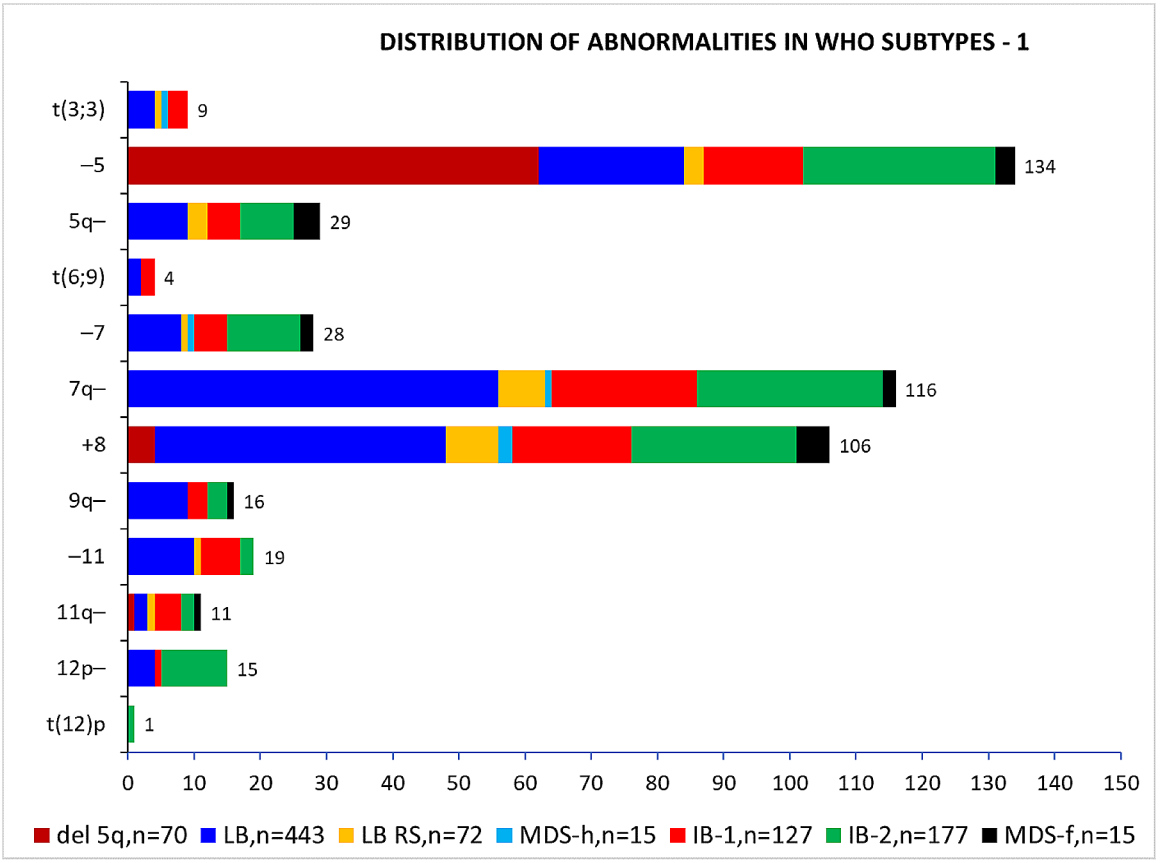


Fig. 3 Karyotypes of some common abnormalities **A**.47,XY,del(5)(q13q33),+21. **B**.46,XX,del(7)(q22q33). **C**.46,XY,del(20)(q12). **D**.45,XY,t(3;3)(q21;q26),-7



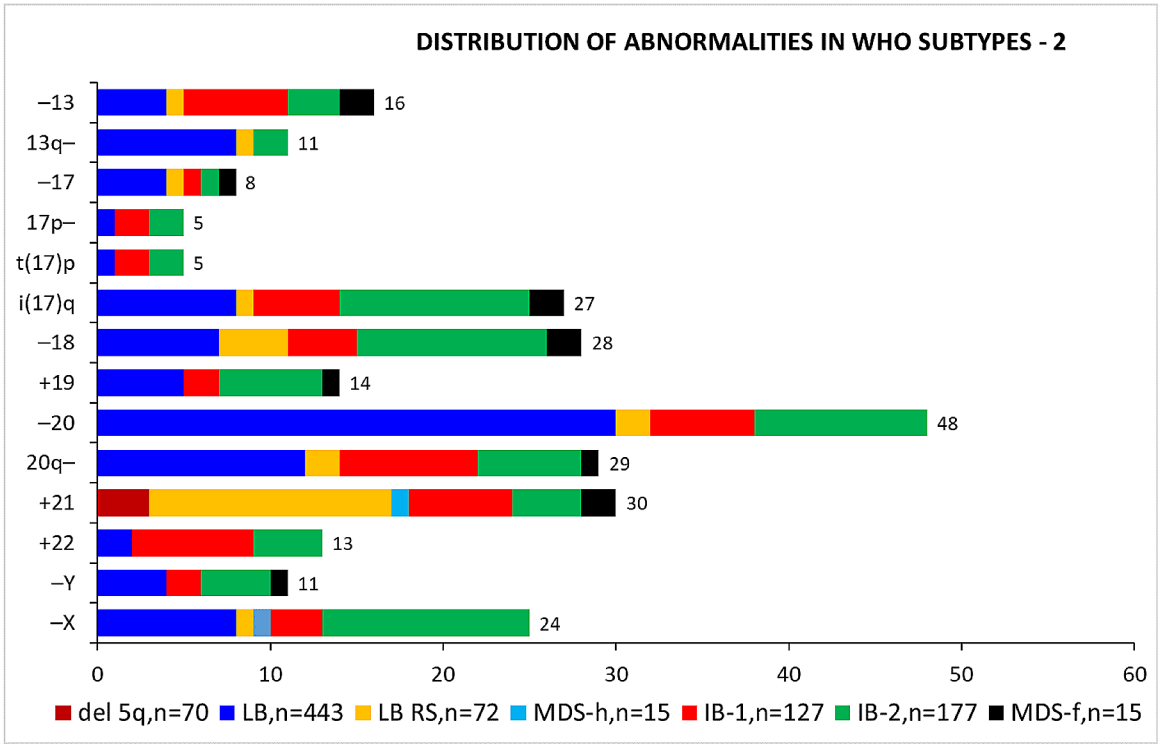


Fig. 4 Distribution of abnormalities in WHO subtypes

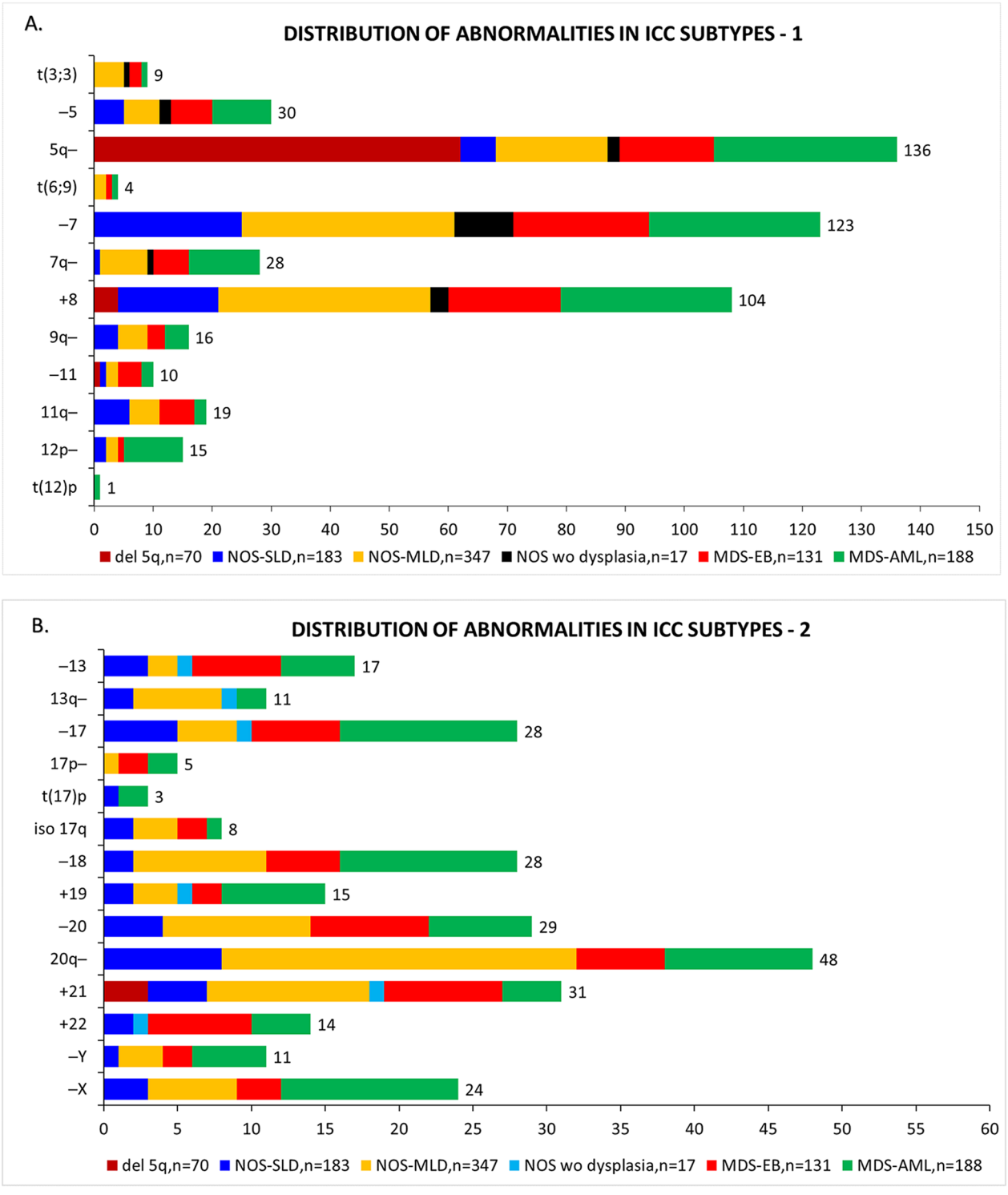


Fig. 5 Distribution of abnormalities in ICC subtypes

Discussion

This first large series of adult patients with primary MDS from South India seen over a 15-year period documents in detail the clinico-pathologic and cytogenetic features and compares our major findings with the literature.

Age and sex distribution (Tables 4 and 5)

The median age of 53 years in this cohort is one to two decades (13–22 years) lower than in reports from the West (66–75 years), as also in Japan (76 years) [12, 14–18, 36–38]. Previous reports from the rest of S.E Asia and

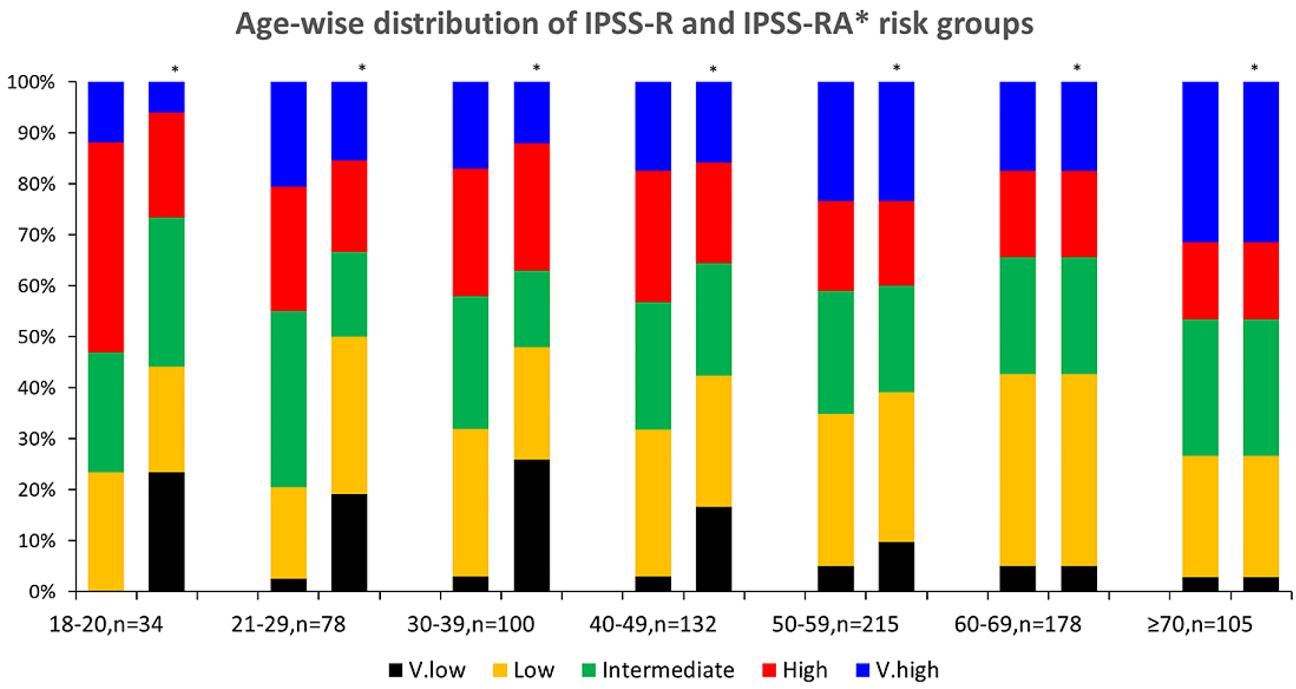


Fig. 6 Age distribution of IPSS-R and IPSS-RA subgroups

Tunisia have recorded a similar age profile (45–57 years and 60 years respectively), two of which (from Tunisia and China) also included children [20–25, 33, 39–41]. The M: F ratio was also comparable to these reports (1.8 vs. 1.3-1.9 in the West and 1.1–2.1 in S.E. Asia and Tunisia [14–25, 28, 33–37, 39, 40]. The median age of our MDS-del 5q (57 years) was also lower than in Europe (65 years); it was more common in females (M: F ratio 0.6 vs. 0.49 and 1.0 in Europe) (Table 2 and Additional File 1) [42, 43].

Cytogenetic abnormalities (Tables 4 and 5, Additional Files 3 & 4)

The frequency of clonal abnormalities varied from 37 to 52% in large (968 to nearly 6000 patients) studies from the West and 35–68% in other studies from Europe, S.E Asia and Tunisia (224–665 patients) [14–23, 25, 33, 36, 37, 39, 40]. However, three of the large Western studies and those from Greece, Tunisia and China included patients with chronic myelomonocytic leukemia (CMML) and refractory anemia with excess blasts in transformation (RAEB-t) which were formerly classified as MDS, secondary MDS and myelodysplastic syndrome/myeloproliferative neoplasm (MDS/MPN) [14–16, 25, 36, 39]. Some also included secondary MDS and myelodysplastic syndrome/myeloproliferative neoplasm (MDS/MPN) [14, 18, 36, 37]. Clonal abnormalities were seen in 55% of our patients.

The del 5q, trisomy 8, monosomy 7/del 7q and del 20q are the most common abnormalities in MDS but their frequencies tend to vary in different parts of the world [1, 2, 19]. The deletion 5q was the most common abnormality in most Western studies followed by trisomy 8, monosomy 7/del 7q and del 20q [14–19, 44].

Trisomy 8 was the most common abnormality in S.E Asia followed by monosomy 20/del 20q, monosomy 7/del 7q and the del 5q. [19–23, 33]. However, the most common abnormalities in this cohort in decreasing order of frequency were monosomy 7/ del 7q, del 5q, trisomy 8, and del 20q.

Comparison of the cytogenetic profiles of our patients with weighted averages from each region showed differences and similarities. The frequencies of monosomy 7/del 7q, del 5q, trisomy 8 and del 20q were higher in our study than in the West. Monosomy 7/del 7q was almost four times as common (16.1% vs. 4.5%), and the del 5q, trisomy 8 and del 20q almost twice, or twice as common (14.5% vs. 8.3%, 11.5% vs. 5.7% and 5.1% vs. 2.5% respectively) as in the West ($P<0.001$). Most of our other abnormalities, namely, del 11q ($P=0.001$), isochromosome 17q ($P=0.017$), der (1;7) ($P=0.004$), abnormalities of chromosome 1, monosomy 13/del 13q, monosomy 17/del 17p, trisomy 19 and trisomy 21 were also more common than in the West ($P<0.001$) but there were no significant differences in the frequencies of 3q abnormalities, del 12p, monosomy 18 / del 18q and minus Y (Additional File 3) [14–19].

Trisomy 8 was more common in S.E Asia than among our patients, its weighted average (14%, $P=0.05$) trending towards significance although its frequency varied

Table 4 Comparison of clinical features and cytogenetic abnormalities in primary MDS in the West, S.E. Asia & Tunisia

Authors	This study	Schanz [15]	Haase [14]	Pozd-nyakova [17]	Solé [16]	Berggren [18]	Miyazaki [19]		Wang [20]	Yan [21]	Li [33]	Qu [22]	Jung [23]	Gmidène [25]
Country	India	Germany & Austria		USA	Spain	Sweden	EU & USA	Japan	China	China	China	China	Korea	**Tunisia**
Year	2023	2012	2007-08	2009	2005	2018	2018	2018	2021	2021	2009	2012	2008	2008
Patients, n	988	2902	2124	1029	968	1329	5838	300	655	634	351	532	231	224
Age, median (range)	53 (18–86)	70 (16–96)	65.7 (0.1–96)	67 (19–92)	70 (1–94)	75 (17–96)	71 (40–106)	65.5 (40–90)	51 (6–86)	57 (18–86)	45 (16–79)	48 (16–81)	51 (18–84)	60 (1–90)
M: F ratio	1.8:1	1.4:1	1.8:1	1.9:1	1.3:1	1.8:1	1.6:1	1.5:1	1.1:1	1.4:1	2.1:1	2:1	2:1	1.4:1
No. of KTs	**936**	**2801**[a]	**2072**[b,^]	**1029**	**968**[c]	**995**[d]	**4844**[e,*]	**261**[e,*]	**665**	**634**	**351**	**532**	**231**	**224**
Normal KT(%)	45	55.1	47.7	55.5	53	49	62.7	65.5	55.2	61.4	32.5	35	49.8	47.2
Clonal abn (%)	55	44.9	52.3^	44.5	47	51	37.3	34.5	44.8	38.6	67.5	65	50.2	52.8
Frequencies of individual abnormalities, %														
Der(1;7)	0.9	0.3	–	0.6	–	–	0.3	1.9	–	–	–	1.9	–	–
Inv/t/del 3q	0.96	0.4	2	0.3	–	0.1	0.4	0.8	0.8	–	0.8	1.9	0.9	0.4
5q–	14.5	6.4	15.1	5.9	5.7	4	8.6	1.9	3.2	10.6**	5.1**	5.8	78	13
–7/ 7q–	13.1/3	1.6/0.5	11.1	0.8/0.9	3/1.4	2	2.7/1.5	1.1/2.7	4.1	7.7	8.8	9	6.9	8
+8	11.5	4.7		3.7	5.8	5	5.8	3.8	11.3	12	19.1	20	17.3	3
11q–	2	0.7	1.1	0.5	–	0.4	1.2	1.1	1.2	2.7^^	2.6	1.9	0.9	–
12p–	1.6	0.6	1.2	0.3	–	0.3	1.3	1.1	–	2.1	1.4	1.9	2.6	4
–13 / 13q–	1.8/1.2	0.3	1.9	–	–	–	0.8	0.8	–	2.8	–	2.6	–	2
i(17)q	0.9	0.4	2.6 with iso 17q	0.2	1	0.2	0.3	0.8	–	–	3.8	3.2	–	1
–17/ 17p–	3/0.5	0.2		–	0.5	–	0.6	1.1	–	–	–	2.6	2.6	–
–18	3	–	3.8^^^	–	–	–	–	–	–	2.5	2.8	3.2	–	–
+19	1.6	0.4	–	0.4	–	0.2	0.5	0	0.5	–	2.8	–	–	0.4
20q–	5.1	1.7	3.6	2.7	1.3	2	2.8	6.9	5.7	6.3	9.4 [#]	7.8	6.5	3
+21	3.3	–	2.2	–	–	–	0.9	–	1.2	–	2.6	2.6	3.5	0.4
–Y	2.6	2.2	2.8	2	1.8	5	3.4	1.1	2.3	2.2	2.3	2.6	2.6	0.4
No. of abnormalities in each karyotype, %														
Single abn	29.8	28.7	29	26.9	35.9	–	–	–	36.5	–	54.8	38	–	–
Two abn	7.5	6.2	9			–	–	–		–	22.8	11	–	–
IncC***	2.7	0.9	–	–	–	–	–	–	–	–	–	–	–	–
All CK****	15	9.1	14	17.6	11	–	–	–	8.3	–	22.4	16	15	8
CK,3 abn	3.8	2.1	3	–	–	–	–	–	–	–	–	4	–	–
CK, > 3 abn	11.2	7	11	–	–	–	–	–	–	–	–	12	–	–
Cytogenetic score (prognosis) categories, %														
						n = 973	*n* = 5838	*n* = 300				*n* = 532		
Very good	2	2.9	–	–	–	6	3.6	1	1.8	–	–	2	–	–
Good	55.6**^	65.7	–	–	–	56	72.2	71.3	61.2	–	–	43	–	–
Intermediate	16.2	19.2	–	–	–	15	13.3	17	25	–	–	36	–	–

Table 4 (continued)

Authors	This study	Schanz [15]	Haase [14]	Pozdnyakova [17]	Solé [16]	Berggren [18]	Miyazaki [19]	Wang [20]	Yan [21]	Li [33]	Qu [22]	Jung [23]	Gmidène [25]
Poor	15	5.4	–	–	–	8	4.1	4.3	7.6	–	–	7	–	–
Very poor	11.2	6.8	–	–	–	15	6.9	6.3	4.4	–	–	12	–	–
	n = 842*^^					*n* = 973	*n* = 5838	*n* = 300						
Very low	3.9	–	–	–	–	13	19.5	10	–	–	–	–	–	–
Low	30.9	–	–	–	–	34	37.7	31.7	–	–	–	–	–	–
Intermediate	24.2	–	–	–	–	20	19.2	32	–	–	–	–	–	–
High	21	–	–	–	–	16	13.1	13.3	–	–	–	–	–	–
Very high	20	–	–	–	–	17	10.5	13	–	–	–	–	–	–

[a], includes 687(23%) chronic myelomonocytic leukemia (CMML) and oligoblastic AML; [b], includes 143 secondary MDS, & 709 (33%) CMML, RAEB-t and MDS-AL; [c], includes 275(28%) CMML and RAEB-t; [d], includes 183 t-MDS; [e], only those ≥ 40 years; KTs, karyotypes; abn, abnormalities; der, derivative; Inv, inversion; –, minus or loss or monosomy; del, deletion; t, translocation; +, plus or trisomy; i, isochromosome; ^, 1931 primary MDS only, with clonal abnormalities in 986 (51.1%); *, numbers used to determine frequency of abnormalities; **, includes monosomy 5; ^^, includes monosomy 11; ^^^, includes del 18q; #, includes monosomy 20; ***, IncC, independent non-complex clones; ****, CK, complex karyotypes; **^, comprises 10.6% abnormal and 45% normal karyotypes; *^^, ≥ 40 years, *n* = 696, used for comparison with Miyazaki et al [19]

widely (4–20%) in individual studies. The isochromosome 17q was also more common (2.3%, $P=0.02$) in S.E Asia, but we had higher frequencies of monosomy 17/del 17p ($P=0.014$). We also had considerably higher (more than twice) frequencies of monosomy 7/ del 7q and del 5q than in S.E Asia (6.8% and 6% respectively $P<0.001$). The frequencies of the del 20q and the other abnormalities were not significantly different from our study (Additional File 3) [19–23, 33].

Minus Y which occurs in MDS, but may also be seen in non-neoplastic marrows of older men, was the most common single abnormality (5%) reported by Berggren et al., with 90% occurring in men > 60 years of age [18]. We found minus Y in 2.6% with 79% seen in those ≥ 40 years, and 33% in those ≥ 60 years. This frequency was comparable to other reports from the West (1.8–3.4%) and Japan (1.1%) which also had older populations than ours, and S.E Asia (2.2–2.6%) [14–17, 19–23] (Table 4).

The frequency of our CKs (15%) was higher than in the West (12.1%, $P=0.011$) although frequencies varied considerably (9-17.6%) in individual studies. There was no significant difference in the weighted average of CKs in S.E Asia (14.5%) although again, wide variations in frequency (8.5–22.4%) were noted in individual studies [14–23, 33]. Independent non-complex clones (IncCs) were seen in 2.7% of our patients compared to 0.9% in the report by Schanz et al. (Table 4 & Additional File 3) [15].

Salient differences between our findings and the report from Tunisia were a lower frequency of the del 12p (1.6% vs. 4%, $P=0.023$) in our study and higher frequencies of monosomy 7/del 7q ($P=0.002$), trisomy 8 ($P<0.001$), trisomy 21 ($P=0.017$), minus Y ($P=0.043$) and CK ($P=0.006$). There were no significant differences in the frequencies of del 5q and the other abnormalities (Table 4 & Additional File 3) [25].

Comparison with other reports from South Asia showed some differences [28, 34, 35]. We had higher frequencies of abnormal karyotypes ($P=0.001$), del 5q ($P<0.001$) and monosomy 7/del 7q ($P<0.001$) and del 20q ($P=0.048$) than in Pakistan while there were no significant differences between the frequencies of trisomy 8 and CK (Additional File 4) [28, 34, 35].

There are several studies from India but most are of small numbers (40–60) of patients and show wide variations in the frequencies of clonal abnormalities (35-64.5%) as well as monosomy 7/del 7q (8–16%), del 5q (3.5–27%) and trisomy 8 (1.2–12.5%); some mainly used FISH and/or included CMML and RAEB-t [29, 30, 45–49]. Comparison with the two largest reports from India (104–150 patients) showed that the frequencies of the del 5q (4.8%, $P=0.0003$) and trisomy 8 (3.2%, $P=0.0005$) were lower than in our study while there were no significant differences with respect to the other abnormalities (Additional File 4) [29, 30]. Being series of relatively small

Table 5 Comparison of clinical features and cytogenetic abnormalities in primary MDS in S.Asia

	This study	Gupta [30]	Vundinti [29]	Anwar [35]	Mahmood [28]	Rashid [34]
Country	India	India	India	Pakistan	Pakistan	Pakistan
Year	2023	2017	2009	2017	2018	2014
No. of patients	988	150	104/160*	177	178	122
Age, median (range)	53(18–86)	55.5(2–87)	44(5 mo-75)	50(3–90)	58(30–85)	60(40–80)
M: F ratio	1.8:1	1.6:1	2.1:1	3.0:1	2.0:1	1.5:1
No. of karyotypes,	**936**	**86**	**104/160***	**98**	**178**	**71**
Clonal abnormalities, %	55.2	50	49	44	46.6	42.3
***Frequencies of individual abnormalities*, %**						
Der (1;7)	0.9	–	–	–	–	–
Inv/t/del 3q	0.96	–	–	–	–	–
5q–	14.5	3.5	5.8	6.1	7.3	2.8
–7/ 7q–	13.1/3	16.3	12.5	7.1/2	6.7 (5.6/1.1)	–/4.2
+8	11.5	1.2	4.8	3.1	12.9	9.9
11q–	2	–	–	–	2.8	1.4
12p–	1.6	–	–	–	–	–
–13/13q–	1.8/1.2	–	–	–	–	–
i(17)q	0.9	–	–	–	0.6	–
–17/17p–	3/0.5	–	2.9	–	–	–
–18	3	–	–	–	–	–
+19	15(1.6)	–	–	–	–	1.4
20q–	5.1	4.7	1.9	4	2.2	1.4
+21	3.3	–	–	1	–	–
–Y	2.6	–	–	–	2.8	2.8
***No. of abnormalities in each karyotype*, %**						
Single abnormality	29.8	19.8	–	–	31.4	19.2
Double abnormalities	7.5	8.1	–	–	4.5	6.7
IncC**	2.7	–	–	–	–	–
All CK	15	16.3	–	12	10.7	16.4
CK with 3 abnormalities	3.8	–	–	–	–	–
CK with > 3 abnormalities	11.2	–	–	–	–	–
***Cytogenetic score (prognosis) categories*, %**						
Very good	2	1.1	–	–	5.6	–
Good	55.6***	56.9	–	–	62.9	–
Intermediate	16.2	11.6	–	–	15.2	–
Poor	15	13.9	–	–	12.9	–
Very poor	11.2	16.2	–	–	3.4	–
***Clinical (IPSS-R) risk groups*, %**						
Very low	3.9	2.3	–	–	9.6	–
Low	30.9	12.8	–	–	41	–
Intermediate	24.2	29	–	–	27.1	–
High	21	31.4	–	–	13.5	–
Very high	20	24.4	–	–	9.1	–

*excluding RAEB-t, CMML and RAEB with t(8;21),$n=41$; i, isochromosome; ** IncC, independent non-complex clones; ***comprises 10.6% abnormal and 45% normal karyotypes

numbers of patients, referral bias could be the reason for these differences. It is also not clear whether consecutive patients were included in those series.

Cytogenetic prognosis groups (Table 6 & Additional File 5)

With 11.2% of very poor prognosis karyotypes in this series, this was higher than in the West, Japan and China (7%, $P<0.001$; 6.3%, $P=0.004$ and 7.8%, $P=0.007$, respectively), while the poor prognosis group was considerably higher (two to three times) than in all three regions (15% vs. 4.3-7%, $P<0.001$). These differences are explained by the higher frequencies of monosomy 7 and CK with >3 abnormalities in our patients [12, 15, 18–20, 22].

The number of karyotypes in each of the other three prognostic groups was lower than in one or more of the other regions. We had almost half the number of

Table 6 Comparison of cytogenetic prognostic groups in MDS

Authors	This study	Schanz [15]	Greenberg [12]	Berggren [18]	Miyazaki [19] (≥ 40 years)		Wang [21]	Qu [22]	Mahmood [28]	Gupta [30]
Year	**2021**	**2012**	**2012**	**2018**	**2018**		**2021**	**2012**	**2018**	**2017**
Country	**India**	**Germany**	**USA**	**Norway**	**Australia**	**Japan**	**China**	**China**	**Pakistan**	**India**
No. of patients	936	2754	7012	973	5838	300	665	532	178	86
Very good prognosis	2	2.9	4	6	3.6	1	1.8	2	5.6	1.1
Good prognosis	55.6	65.7	72	56	72.2	71.3	61.2	43	62.9	56.9
Normal karyotypes	45	*55.1*	*NA*	*49*	*62.7*	*65.3*	*55.2*	*35*	*53.4*	*50*
Intermediate prognosis	16.2	19.2	13	15	13.3	17	25	36	15.2	11.6
Poor prognosis	15	5.4	4	8	4.1	4.3	7.6	7	12.9	13.9
Very poor prognosis	11.2	6.8	7	15	5.9	6.3	4.4	12	3.4	16.2

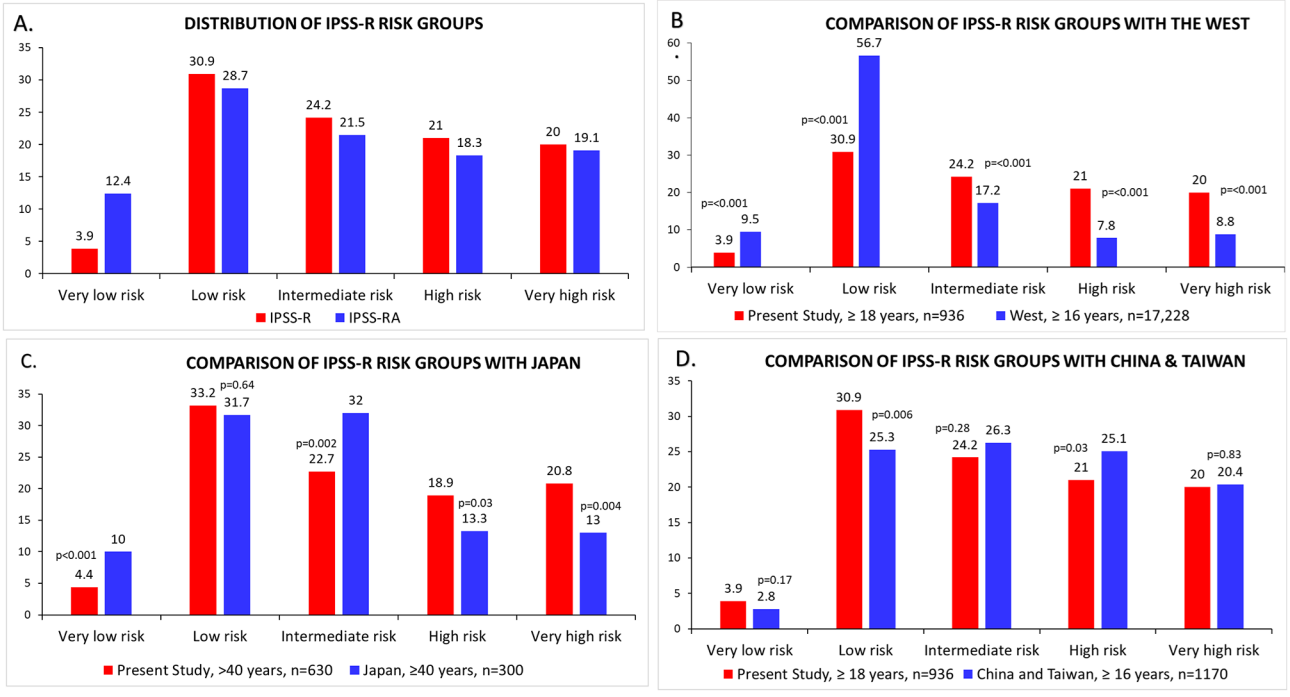


Fig. 7 **A**. Distribution of IPSS-R and IPSS-RA risk groups. **B**. Comparison of IPSS-R risk groups with the West. **C**. Comparison of IPSS-R risk groups with Japan. **D**. Comparison of IPSS-R risk groups with China and Taiwan

karyotypes in the intermediate prognosis group as in China (16% vs. 30%, $P<0.001$), fewer karyotypes in the good prognosis group than in the West and Japan ($P<0.001$), and in the very good prognosis group than in the West ($P=0.005$). These differences could be reflective of the frequency of trisomy 8 (intermediate prognosis) which was the most common abnormality in China, and the lower frequency of normal karyotypes (good prognosis) in our study compared to the West and Japan. The difference in the frequency of the very good prognosis group could possibly be due to the considerably higher frequency of minus Y in the study by Berggren et al. (Table 6 and Additional File 5) [12, 15, 18–20, 22].

Only two studies from South Asia (one each from India and Pakistan) described the cytogenetic prognosis groups [28, 30]. The study from Pakistan had more karyotypes in the very good (5.6%, $P=0.006$) prognosis group and fewer karyotypes in the very poor prognosis group ($P=0.001$). However, the frequencies of all five prognosis groups were comparable to the other study from India. (Tables 6 *and* Additional File 5).

Clinical risk groups (Figs. 6 and 7)

The distribution of clinical risk groups also varies in different parts of the world (Fig. 7.B, C, D). There were highly significant differences between Western studies (age≥16 years, $n=17,228$) and our study ($n=842$) with respect to all five clinical risk groups ; we had fewer patients in both low-risk groups (34% vs. 66%) and more patients in the intermediate-risk (24% vs. 17%) and both high-risk (41% vs. 17%) groups ($P=<0.001$) [12, 16, 18, 50–52].

Comparison with a study from Japan (age≥40 years, $n=300$ vs. $n=630$ aged≥40 years in our study) also showed that we had more patients in our high-risk (19% vs. 13%, $P=0.03$) and very high-risk (21% vs. 13%, $P=0.004$) groups and fewer patients in the very low-risk (4.4% vs. 10%, $P < 0.001$) and intermediate-risk (23% vs. 32%, $P=0.002$) groups [19].

We had significantly more patients in the low-risk (31% vs. 25%, $P=0.006$) group and fewer patients in the high-risk (21% vs. 25%, $P=0.03$) group than in studies from China and Taiwan (age≥16 years, $n=1170$) [21, 53, 54].

This study has some limitations with respect to the lack of molecular studies and clinical follow-up. However, we believe that this report still brings out the lower age as well as the high frequency of complex karyotypes and poor prognosis markers in this population and will remain relevant with the updated WHO 2022 and ICC 2022 based classifications of entities included. Our data also provides a detailed description of the spectrum of cytogenetic abnormalities in MDS.

Conclusion

This large series of adult patients with MDS from India has several unique features. Apart from confirming the significantly lower age at presentation in India, it also documents the higher frequencies of monosomy 7, both poor prognosis groups and the IPSS-R high-risk groups among these younger patients than in the West. The reasons for these differences are unclear and could reflect differences in environmental exposures particularly to widely used pesticides and fertilisers, as well as possible genetic predispositions. Molecular analysis and detailed epidemiological studies would help in the identification of such predisposing factors, both inherited and environmental, and early recognition for more effective therapeutic interventions.

Abbreviations

abn	abnormality/abnormalities
AML	Acute myeloid leukemia
CK	complex karyotype(s)
ANC	absolute neutrophil count
CMML	chronic myelomonocytic leukemia
CCSS	comprehensive cytogenetic scoring system
CK	complex karyotype
del	deletion
der	derivative
FISH	fluorescence in situ hybridization
Hb	haemoglobin
ICC	International Consensus Classification of Acute Myeloid Leukemia
IncC	independent non-complex clones
inv	inversion
IPSS-R	Revised International Prognostic Scoring System
IPSS-RA	Age-adjusted Revised International Prognostic Scoring System
i	isochromosome
Intrmdt	intermediate
M:F ratio	male:female ratio
mar	marker chromosomes
MK	monosomal karyotype(s)
MDS	myelodysplastic syndrome
MDS-f	MDS with fibrosis
MDS-h	MDS, hypoplastic
MDSLB	MDS with low blasts
MDS-LB-RS	MDS with low blasts and ring sideroblasts
MDS-NOS-SLD	MDS, not otherwise specified, with single lineage dysplasia
MDS-NOS-MLD	MDS, not otherwise specified, with multilineage dysplasia
MDS wo dyspl	MDS without dysplasia
MDS-EB	MDS with excess blasts
MDS-IB	MDS with increased blasts
Plt	platelet count
RAEB-t	refractory anaemia with excess blasts in transformation
S.Asia	South Asia
S.E.Asia	South-East Asia
t	translocation
UK	United Kingdom
USA	United States of America
WHO	World Health Organisation

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13039-024-00687-z.

Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

Supplementary Material 4

Supplementary Material 5

Acknowledgements

We thank Dr. Bijesh Yadav for his valuable suggestions regarding statistical analysis.

Author contributions

VMS: design, manuscript preparation, cytogenetic analysis, data analysis; SCN, MTM: Morphologic analysis, manuscript review; MJ, KML: Statistical analysis, data analysis; UPK, AK, AA: clinical data acquisition, manuscript review; AJD, FNA: clinical data acquisition, manuscript editing and review; LJ: Statistical analysis, manuscript review; AS: clinical data acquisition, literature search, manuscript editingand review. All authors have read and approved the manuscript.

Funding information

No funding was received for conducting this study.

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was performed in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of the Christian Medical College, Vellore : IRB minute no. 13082 [Retro] June 2020.

Consent for publication

Approval for retrospective analysis granted by the Institutional Review Board of the Christian Medical College, Vellore as per institutional policy.

Competing interests

The authors declare that they have no competing interests.

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Received: 8 January 2024 / Accepted: 15 July 2024
Published online: 27 September 2024

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