Hematology/Oncology and Stem Cell Therapy

Volume 15 | Issue 2 Article 6

Spectrum of Myelodysplastic Syndrome in Patients Evaluated for Cytopenia(s). A Report from a Reference Centre in Saudi Arabia

Nour AlMozain
Department of the Blood Bank, King Saud University Medical City, King Saud University, Riyadh, Saudi Arabia, nalmozain@ksu.edu.sa

Ayman Mashi
Department of Laboratory and Bloo Bank, King Fahad Central Hospital, Ministry of Health, Jazan, Saudi Arabia

Qasem Alneami
Department of Laboratory and Bloo Bank, King Fahad Central Hospital, Ministry of Health, Jazan, Saudi Arabia

Amal Al-Omran
Medical student, King Saud University, College of Medicine, Riyadh, Saudi Arabia

Nasir Bakshi
Department of Pathology and Laboratory Medicine, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia

See next page for additional authors

Follow this and additional works at: https://www.hosct.org/hematology-oncology-and-stem-cell-therapy

Part of the Cancer Biology Commons, Hematology Commons, and the Oncology Commons

Recommended Citation

AlMozain, Nour; Mashi, Ayman; Alneami, Qasem; Al-Omran, Amal; Bakshi, Nasir; Owaidah, Tarek; Khalil, Salem; Khogeer, Haitham; Hashmi, Shahrukh; Al-Sweedan, Suleimman; Morris, Thomas; and AlNounou, Randa (2022) "Spectrum of Myelodysplastic Syndrome in Patients Evaluated for Cytopenia(s). A Report from a Reference Centre in Saudi Arabia," *Hematology/Oncology and Stem Cell Therapy*: Vol. 15 : Iss. 2 , Article 6.
Available at: https://doi.org/10.1016/j.hemonc.2020.11.001

This Original Research Report is brought to you for free and open access by Hematology/Oncology and Stem Cell Therapy. It has been accepted for inclusion in Hematology/Oncology and Stem Cell Therapy by an authorized editor of Hematology/Oncology and Stem Cell Therapy.

Spectrum of Myelodysplastic Syndrome in Patients Evaluated for Cytopenia(s). A Report from a Reference Centre in Saudi Arabia

Authors

Nour AlMozain, Ayman Mashi, Qasem Alneami, Amal Al-Omran, Nasir Bakshi, Tarek Owaidah, Salem Khalil, Haitham Khogeer, Shahrukh Hashmi, Suleimman Al-Sweedan, Thomas Morris, and Randa AlNounou

This original research report is available in Hematology/Oncology and Stem Cell Therapy: https://www.hosct.org/hematology-oncology-and-stem-cell-therapy/vol15/iss2/6

ORIGINAL RESEARCH REPORT

Spectrum of Myelodysplastic Syndrome in Patients Evaluated for Cytopenia(s). A Report from a Reference Centre in Saudi Arabia

Nour AlMozain [a], Ayman Mashi [b], Qasem Alneami [b], Amal Al-Omran [c], Nasir Bakshi [d], Tarek Owaidah [d], Salem Khalil [d], Haitham Khogeer [d], Shahrukh Hashmi [e], Suleimman Al-Sweedan [f], Thomas Morris [d], Randa AlNounou [d,*]

[a] Department of the Blood Bank, King Saud University Medical City, King Saud University, Riyadh, Saudi Arabia
[b] Department of Laboratory and Bloo Bank, King Fahad Central Hospital, Ministry of Health, Jazan, Saudi Arabia
[c] Medical student, King Saud University, College of Medicine, Riyadh, Saudi Arabia
[d] Department of Pathology and Laboratory Medicine, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia
[e] Department of Medicine, Sheikh Shakbout Medical City, Abu Dhabi, United Arab Emirates
[f] Department of Pediatrics, Jordan University of Science and Technology, Irbid, Jordan

Abstract

Background/Objective: **Myelodysplastic syndrome (MDS) is a clonal disorder of hematopoietic stem cells, characterized by ineffective hematopoiesis, peripheral cytopenias along with hypercellularity of the bone marrow, and marked dysplastic features. Establishing MDS diagnosis is difficult due to nonspecific clinical presentation and imprecise morphological criteria. In anticipation to improve the diagnostic approach in this field, we aimed to characterize the clinical and morphological features of patients presented with cytopenias with a special focus on MDS.**

Methods: **We comprehensively reviewed all medical record of patients who were referred to the hematology laboratory at KFSH-RC, Riyadh, Saudi Arabia, between January 2009 and March 2016 for evaluation of bone marrow aspirates and trephine biopsies due to severe and persistent cytopenia(s) to rule out MDS.**

Results: **A total of 183 patients, 155 adult and 28 pediatric, were identified. In the adult group, MDS was diagnosed in 82 (52.9%) patients, with a male-to-female (M:F) ratio of 1.6:1 and mean age at diagnosis of 50 years. According to the World Health Organization (WHO) 2017 criteria, MDS subtypes were as follows: MDS with single lineage dysplasia (SLD, 5%), MDS with ring sideroblasts and SLD (MDS-RS-SLD 7%), MDS with multilineage dysplasia (MDS-MLD 21%), MDS with deletion of chromosome 5q (MDS del(5q), 2%), MDS unclassifiable (MDS-U7%), hypoplastic MDS (h-MDS 4%), MDS with excess blasts-1 (MDS-EB1, 20%), MDS with excess blasts-2 (MDS- EB2, 28%), and therapy-related MDS (6%). Laboratory and morphological features were described. In both groups, cytogenetic abnormalities were classified according to the Revised International Prognostic Scoring System cytogenetic risk groups. In adults, the dominating cytogenetic abnormalities were monosomy 5 and monosomy 7 seen in 20.7% and 24.4% of patients, respectively. Peripheral cytopenia not due to MDS was diagnosed in 54 (34.8%) patients, with a mean age of 43 years and M:F ratio of 1:1. The cause of these cytopenias were as follows: bone marrow failure (BMF, 22%), peripheral destruction (20%), drug induced (20%), anemia of chronic disease (16%), B12 deficiency (7%), infection (7%), paroxysmal nocturnal hemoglobinuria (4%), idiopathic cytopenia of undetermined significance (2%), and idiopathic dysplasia of undetermined significance (2%). A definite diagnosis of MDS was not possible in 19 patients due to insufficient clinical data. In the pediatric group, MDS was diagnosed in 14/28 (50%) patients, with M:F ratio of 1.8:1 and mean age at diagnosis of 4 years. MDS subtypes (WHO 2017) in 14 patients were as follows: refractory cytopenia of childhood (RCC, 42.8%), MDS-EB1 (42.8%), and MDS-EB2 (14.2%). Laboratory and morphological features were described. The prevalent cytogenetic abnormality was monosomy 7 in six/14 (42.8%) patients. Cytopenias due to other causes were diagnosed in eight/28 patients (28.5%), with a mean age of 6.5 years and M:F ratio of 1.6:1. The causes of non-MDS related cytopenia were: congenital BMF (4 patients), peripheral**

Received 27 June 2020; revised 12 October 2020; accepted 3 November 2020.
Available online 1 June 2022

* Corresponding author at: Department of Pathology and Laboratory Medicine, King Faisal Specialist Hospital, P.O. Box 3354, Riyadh, Saudi Arabia.
E-mail addresses: nalmozain@ksu.edu.sa (N. AlMozain), sweedan@just.edu.jo (S. Al-Sweedan), nounou@kfshrc.edu.sa (R. AlNounou).

https://doi.org/10.1016/j.hemonc.2020.11.001
2589-0646/© 2022 King Faisal Specialist Hospital and Research Centre. This is an open access article under the CC-BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

destruction (2 patients), immune deficiency (1 patient), and viral infection (1 patient). A definite diagnosis of MDS could not be made in six/28 (21.4%) patients.

Conclusion: **MDS is the cause of cytopenia in a significant number of patients referred for evaluation of cytopenias, appears at younger age, and tends to be more aggressive than that reported in international studies. Anemia, dysplastic neutrophils in the peripheral blood, and dysplastic megakaryocytes in the bone marrow trephine biopsy are the most reliable features in distinguishing MDS from other alternative diagnoses.**

Keywords: Cytopenias, Myelodysplastic syndrome (MDS), Myelodysplastic syndrome

1. Introduction

Myelodysplastic syndrome (MDS) is a clonal disorder of hematopoietic stem cells, characterized by ineffective hematopoiesis, peripheral cytopenias along with hypercellularity of the bone marrow, and dysplastic features that could be associated with variable cytogenetic and molecular abnormalities causing bone marrow failure (BMF) with a possible risk of evolution to acute myeloid leukemia [1]. It usually affects older adults, with a median age at diagnosis of ≥65 years and male predominance [2]. Onset of the disease earlier than the age of 50 years is unusual [3]. Rare cases of MDS have been reported in children at a median age of 6 years [4]. In the United States, incidence of the disease is estimated to be between 5.3 and 13.1 per 100,000 people [5], while in Japan, it varies between 1.2 and 2.5 per 100,000 people [6]. Few reported data from Middle East are available [7–10]. Statistics from Saudi Arabia are lacking.

Signs and symptoms of MDS at presentation are nonspecific. Many patients are asymptomatic at diagnosis and only come to the physician's attention based upon abnormalities found on routine blood counts (e.g., anemia, neutropenia, and thrombocytopenia). Others present with symptoms or complications resulting from a previously unrecognized cytopenia (e.g., infection and fatigue). Furthermore, there is no precise morphological criteria for making the diagnosis; dysplasia can be found in a wide range of differential diagnoses such as in vitamin B12 deficiency, viral infection, copper deficiency, or zinc excess.

2. Materials and methods

We comprehensively reviewed all medical record of patients who were referred to the hematology laboratory at KFSH-RC, Riyadh, Saudi Arabia, between January 2009 and March 2016 for evaluation of bone marrow aspirates and trephine biopsies due to severe and persistent cytopenia(s) to rule out MDS. The World Health Organization (WHO, 2017) criteria for classification and nomenclature of MDS was applied.

2.1. Cytogenetic analysis

2.1.1. Karyotype

Bone marrow cells were processed for karyotype analysis according to standard cytogenetic procedures. Heparinized bone marrow aspirate samples were cultured overnight in 25 cm2 culture flasks (Falcon, USA) at 37°C and 5% CO2. After incubation, cultures were transferred to a 15 ml Falcon conical tube and incubated for 1 hour with ethidium bromide (Sigma-Aldrich), washed, and incubated for 1 hour in an in-house prepared Cancer hypotonic solution all at 37°C. Followed by fixation in 3 washes of 3:1 Carnoys fixative (Methanol: Acetic acid) followed by refrigeration. Slides are prepared in a slide drying chamber (Thermotron, USA) aged at 60°C for 2 hours then GTG banded (G band with Trypsin - Giemsa, Sigma Aldrich). Analysis was performed using the GENASIS (Applied Spectral Imaging, USA) software platform. Chromosomal abnormalities were identified and described according to the International System of Human Cytogenetic Nomenclature (ISCN) [11].

2.2. Fluorescence in situ hybridization

Circle slides of 18 mm were prepared from fixed cell suspensions obtained from standard harvest procedures. Slides were aged in a 2x Saline-Sodium Citrate (SSC) (Saline-Sodium Citrate) solution, pretreated with pepsin A solution, and dehydrated in a 70%, 85%, and 100% ethanol series. Slides and the fluorescently labeled DNA probe were co-denatured on Hybrite for 3 minutes at 73 °C and hybridized overnight at 37 °C. The next morning the slides were washed in 0.4% SSC/0.3% NP40 solution at 72 °C, counterstained with 4′,6-diamidino-2-phenylindole (DAPI) (4′,6-diamidino-2-phenylindoleto) visualize the nuclei, and analyzed by fluorescent microscopy. The current MDS fluorescence in situ hybridization (FISH) panel consists of the following Abbott molecular (Vysis) probes: EGR1/D5S23

(5q32/5p15.2), D7Z1/D7S522 (7cen/7q31), D7Z1/D8Z2 (7cen/8cen), 20p/D20S108 (20q12), and RPN1/MECOM (3q21/3q26).

2.3. Statistical analysis

Statistical analysis was performed using SPSS version 20 (SPSS Inc., Chicago, IL, USA). Descriptive statistics for the continuous variables are reported as mean ± standard deviation, and categorical variables are summarized as frequencies and percentages. Categorical variables were compared using chi-square test, and continuous variables were compared using Student t test and Mann–Whitney U test. Hazard ratio was calculated to identify the independent variables that contribute significantly to major outcomes. A p value of <0.05 was considered as the cut-off for significance.

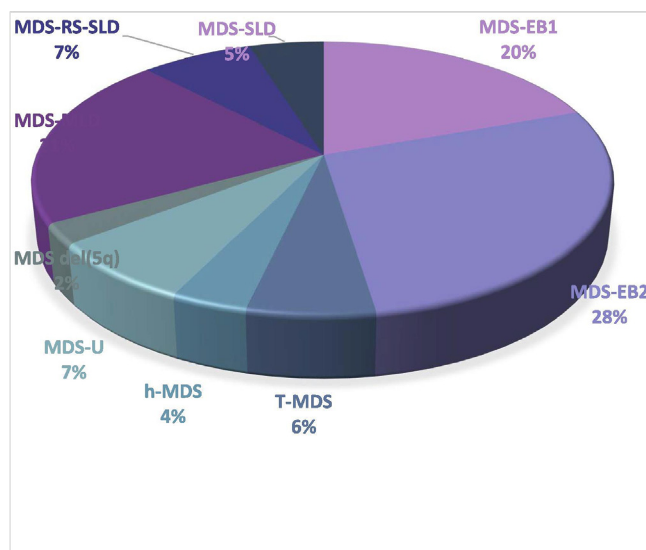

Fig. 1. Myelodysplastic syndrome subtypes. Note. del(5q) = deletion of chromosome 5q; EB1 and 2, excess blasts 1 and 2; h-MDS = hypoplastic myelodysplastic syndrome; MDS = myelodysplastic syndrome; MDS-U = myelodysplastic syndrome unclassifiable; MLD = multilineage dysplasia; RS = ringed sideroblasts; SLD = single lineage dysplasia; T-MDS = therapy-related myelodysplastic syndrome.

3. Results

A total of 183 patients, 155 adult and 28 pediatric, were identified from this review. In the adult group, a diagnosis of MDS was confirmed in 82 (52.9%) patients, with the male-to-female (M:F) ratio of 1.6:1 and a mean age at diagnosis of 50 years. MDS subtypes according to the WHO 2017 criteria were as follows: MDS with single lineage dysplasia (SLD, 5%), MDS with ring sideroblasts and SLD (7%), MDS with multilineage dysplasia (21%), MDS with deletion of chromosome 5q (2%), MDS with excess blasts-1 (EB1, 20%), MDS with excess blasts-2 (EB2, 27%), MDS unclassifiable (7%), hypoplastic MDS (4%), and therapy-related MDS 6%, as shown in Fig. 1. MDS group tended to have lower hemoglobin (≤90 g; $p < .001$; hazard ratio [HR] 0.97; 95% confidence interval [CI]: 0.96–0.98) than non-MDS group (Table 1). In MDS group, the mean absolute neutrophil count (ANC) was 2.17×10^9/L and the mean platelet count was 32.51×10^9/L; these values were comparable with those of non-MDS group (Table 1). Morphological characteristics listed in Table 2 indicate that peripheral blood neutrophils show more evident dysplasia ($p < .001$; HR 5.6; 95% CI: 2.3–8.8), and the morphology of the bone marrow trephine biopsy shows dysplastic megakaryocytes ($p < .001$; HR 5; 95% CI: 1.7–8.2). Dyserythropoiesis, dysgranulopoiesis, and dysmegakaryopoiesis were significantly higher in MDS group than in non-MDS group (70.4%, 79.3%, 59.8% vs. 51.8%, 25.9%, 22.2%, respectively), with $p < .001$ and HR (95% CI) of 2.3 (1.3–3.3), 3.8 (1.9–5.6), and 2.8 (1.5–4.1), respectively. In the MDS group, monosomy 5 and monosomy 7 were the most frequent cytogenetic abnormalities found in 20.7% and 24.4% patients, respectively; they were prevalent in both high-grade MDS and therapy-related MDS, while trisomy 8 and 20q12 were prevalent in low-grade MDS and hypoplastic MDS (Fig. 2). Table 3 presents the Revised International Prognostic Scoring System (IPSS-R) cytogenetic risk group stratification: very good risk (1.2%), good risk (35.4%), intermediate risk (13.4%), poor risk (19.5%), and very poor risk (13.4%). Fig. 3 illustrates the

Table 1. Clinical and laboratory features of myelodysplastic syndrome (MDS) versus non-MDS adult groups.

	MDS	Non-MDS	p; HR (95% CI)
Group size, n	82	54	
M:F ratio	1.6:1	1:1	
Age, mean (SD), years	50 (±18)	43 (±18)	0.035; 1.02 (1.002–1.03)
Hemoglobin, mean, g/dL	90	104	0.001; 0.97 (0.96–0.98)
Absolute neutrophil count, mean, $\times 10^9$/L	2.17	4.47	0.167; 0.91 (0.76–1.6)
Platelet count, mean, $\times 10^9$/L	32.51	29.32	0.429; 1 (0.08–1.2)

Note. CI = confidence interval; F = female; HR = hazard ratio; M = male; SD = standard deviation.

Table 2. Morphological features of myelodysplastic syndrome (MDS) versus non-MDS groups.

	MDS (%)	Non-MDS (%)	*p*; HR (95% CI)
Dysplasia in peripheral blood	84.9	14.81	0.001; 5.6 (2.3–8.8)
Dyserythropoiesis bone marrow aspirate	70.4	51.85	0.001; 2.3 (1.3–3.3)
Dysgranulopoiesis bone marrow aspirate	79.4	25.93	0.001; 3.8 (1.9–5.6)
Dysmegakaryopoiesis bone marrow aspirate	59.8	22.22	0.001; 2.8 (1.5–4.1)
Dysplastic megakaryocytes in bone marrow trephine biopsy	83.3	14.81	0.001; 5 (1.7–8.2)

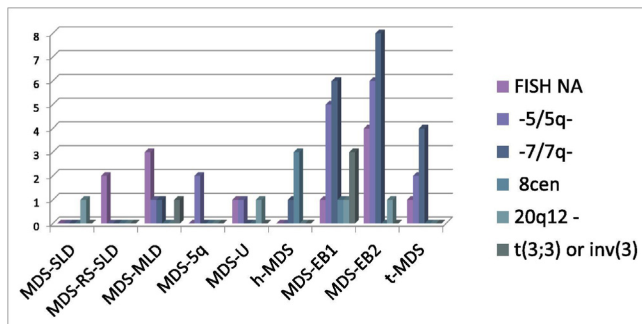

Fig. 2. Results of fluorescence in situ hybridization (FISH) in adult patients with myelodysplastic syndrome. Note. EB1 and 2, excess blasts 1 and 2; h-MDS = hypoplastic myelodysplastic syndrome; MDS = myelodysplastic syndrome; MDS-U = myelodysplastic syndrome unclassifiable; MLD = multilineage dysplasia; RS = ringed sideroblasts; SLD = single lineage dysplasia; T-MDS = therapy-related myelodysplastic syndrome.

Table 3. Revised international prognostic scoring system cytogenetic risk groups.

	Saudi (%)	Japan (%)	Caucasian (%)
Very good	1.2	1	3.6
Good	35.4	71.3	72.2
Intermediate	13.4	17	13.3
Poor	19.5	4.3	4.1
Very poor	13.4	6.3	6.9

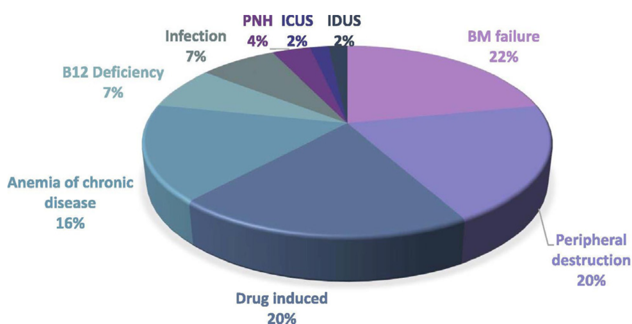

Fig. 3. Diagnosis of non-myelodysplastic syndrome group. Note. BM = bone marrow; ICUS = idiopathic cytopenia of undetermined significance; IDUS = idiopathic dysplasia of undetermined significance; PNH = paroxysmal nocturnal hemoglobinuria.

reasons for peripheral cytopenia that were not due to MDS. Despite suspicious morphology, a definite diagnosis of MDS was not possible in 19 patients due to insufficient clinical data and normal cytogenetics.

In the pediatric group, the results were only descriptive due to the small sample size (Table 4). MDS was diagnosed in 14/28 (50%) patients, with a mean age of 4 years and M:F ratio of 1.8:1. MDS subtypes (WHO 2017) were as follows: six/14 (42.8%) refractory cytopenia of childhood (RCC), six/14 (42.8%) MDS-EB1, and two/14 (14.2%) MDS-EB2. The dominating cytogenetic abnormality was monosomy 7 found in six/14 (42.8%) patients. Another two patients (25%) had a complex karyotype. Two/14 patients showed aberrations involving chromosome 12p by FISH, one with loss of 12p13 and one with a rearrangement involving ETV6 (12p13), but a normal karyotype. Normal cytogenetics were found in five/14 (35.7%) patients. Cytogenetic abnormalities were classified according to IPSS-R cytogenetic risk group as following: good risk six/14 (42.8%), intermediate risk one/14 (7.2%), and poor risk seven/14 (50%) (Fig. 4). MDS was de novo in 10/14 (71.4%) patients and secondary to congenital BMF in four/14 (28.6%) patients. Cytopenia due to other causes was diagnosed in eight/28 (28.5%) patients, with a mean age of 6.5 years and M:F ratio of 1.6:1. The causes of cytopenia were as following: congenital BMF (4 patients), peripheral destruction (2 patients), immune deficiency (1 patient), and viral infection (1 patient). A definite diagnosis of MDS could not be made for six/28 (21.4%) patients.

4. Discussion

To the best of our knowledge, this is the first study in Saudi Arabia that addresses clinical, morphological, and cytogenetic features of MDS. The onset of MDS at a younger age has been more frequently reported in Asian countries, including Japan, China, Korea, India, Thailand, and Turkey, with the median age of patients reported between 40 and 50 years; this is one to two decades younger than that of patients in Western countries [12]. These findings were also confirmed in our study. Environmental pollutions and/or other factors, including uncontrolled pesticide use, may contribute to these differences [12].

The presence of at least one cytopenia is a "*sine qua non*" for any MDS diagnosis; the thresholds are hemoglobin < 10 g/dL, platelet count < 100×10^9/L,

Table 4. Clinical and laboratory features of myelodysplastic syndrome (MDS) versus non-MDS pediatric groups.

	MDS	Non-MDS
Group size, *n*	14 6 RCC - 6 MDS-EB1 - 2 MDS-EB2	8- 4 congenital bone marrow failure - 2 peripheral destruction - 1 immune deficiency - 1 viral infection
Mean age, years	4	6.5
M:F ratio	1.8:1	1.6:1
Hemoglobin, mean, g/dL	72.5	79.7
Absolute neutrophil count, mean, $\times 10^9$/L	0.3258	2.1
Platelet count, mean, $\times 10^9$/L	88.5	197.8

Note. EB1 = excess blasts-1; EB2 = excess blasts-2; F = female; M = male; RCC = refractory cytopenia of childhood.

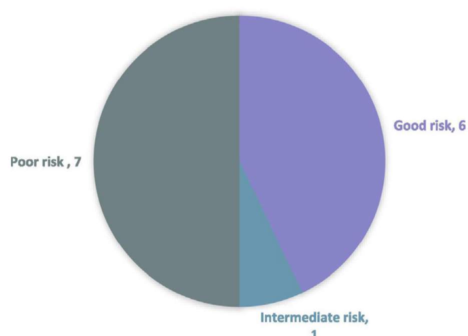

Fig. 4. Revised International Prognostic Scoring System (IPSS-R) cytogenetic risk groups for pediatric patients.

and ANC $< 1.8 \times 10^9$/L [13]. Our findings suggest that among those parameters, anemia with a hemoglobin level < 90 g/dl ($p < .001$) is the most reliable indicator for making the diagnosis.

Morphological abnormalities in red blood cells (RBCs) is usual, including the presence of circulating nucleated RBCs with stigmata of dyserythropoiesis. Dysgranulopoiesis in neutrophils is variably observed, from absent to severe, and can involve both the nucleus and cytoplasm. The nucleus can show abnormal lobulation and/or an abnormal chromatin pattern, while the cytoplasm can show abnormalities in granule size (pseudo-Chédiak–Higashi) and/or content (hypogranular or agranular cytoplasm). Abnormal topographic distribution of the megakaryocytes in the bone marrow trephine biopsy along with features of dysmegakaryopoiesis in bone marrow aspirate, such as multinuclearity, nuclear hypolobulation, and the presence of micromegakaryocytes, are frequently observed in MDS [14]. Our study showed that when dysplastic features are present in the peripheral blood, the diagnosis of MDS is likely if there is high index of clinical suspicion ($p < .001$, HR 5.6). It also emphasizes the importance of the bone marrow trephine biopsy not only for structural assessment but also for morphological evaluation of megakaryocytes to support the diagnosis ($p < .001$, HR 5).

For MDS sub-classification, our patients tended to have more aggressive presentation than the Caucasian and Japanese cohorts (Table 3). High-grade MDS accounted for 45% in our patients compared with 36.4% in Caucasians and 31.8% in Japanese. Del(5q) accounted for 2% in our patients compared with 1.3% in Japanese and 4.7% in Caucasians [15]. When we applied the WHO 2016 sub-classification on the retrospective review, we took into consideration the changes made in the criteria for diagnosis of acute erythroid leukemia. Subsequently, two patients initially diagnosed as acute erythroid leukemia were reclassified as MDS-EB.

Regarding the cytogenetic abnormalities, monosomy 5 and monosomy 7 were the most frequent abnormalities, being prominent in high-grade and therapy-related MDS. The percentage of MDS with normal cytogenetics was significantly lower in our patients (32.9%) than in Japanese (65.3%) and Caucasian (62.7%) cohorts. One explanation for these differences is that most of the high-grade MDS are referred to our center for stem cell transplant. The distribution of IPSS-R cytogenetic risk group was higher in poor and very poor risk groups when compared with the frequency in Japanese and Caucasians [15] (Table 3). The IPSS-R classification was not obtained for 17% of patients due to unavailable genetic data.

The number of pediatric patients was relatively small to draw a statistically significant conclusion. However, the collected data are comparable with a previously published data [16], from King Faisal Specialist Hospital & Research Center between 1993 and 2008, where the mean age was 4.8 years compared with 4 years in our data. Furthermore, RCC was diagnosed in 64% of patients in the previous data compared with 42.8% patients in our data. High-grade MDS has increased compared with the previous data; MDS-EB was diagnosed in

36% of patients compared with 57% of patients in our data. The presence of monosomy 7 was higher in our data than in the previous data (42.8% vs. 35%) [16].

In conclusion, MDS is the cause of cytopenia(s) in a significant number of patients, appears at a younger age, and tends to be more aggressive than that reported in international studies. Anemia, dysplastic neutrophils in the peripheral blood, and dysplastic megakaryocytes in the bone marrow trephine biopsy are the most reliable features in distinguishing MDS from an alternative diagnosis. We recommend future large-scale multicentric studies to include larger number of patients with molecular genetic data for better characterization of this disease entity in the Saudi population.

Declaration of Competing Interest

No conflict of interest to be declared by all authors.

Acknowledgments

We would like to thank Mr. Mohammed Shukri and Mrs. Areej AlFattani for their valuable statistical analysis.

References

[1] Cazzola M. Introduction to a review series: the 2016 revision of the WHO classification of tumors of hematopoietic and lymphoid tissues. Blood 2016;127:2361−4.
[2] Sekeres MA, Schoonen WM, Kantarjian H, List A, Fryzek J, Paquette R, et al. Characteristics of US patients with myelodysplastic syndromes: results of six cross-sectional physician surveys. J Natl Cancer Inst 2008;100:1542−51.
[3] Kuendgen A, Strupp C, Aivado M, Hildebrandt B, Haas R, Gattermann N, et al. Myelodysplastic syndromes in patients younger than age 50. J Clin Oncol 2006;24:5358−65.
[4] Bader-Meunier B, Miélot F, Tchernia G, Buisine J, Delsol G, Duchayne E, et al. Myelodysplastic syndromes in childhood: report of 49 patients from a French multicentre study. Br J Haematol 1996;92:344−50.
[5] Cogle CR. Incidence and burden of the myelodysplastic syndromes. Curr Hematol Malig Rep 2015;10:272−81.
[6] Chihara D, Ito H, Katanoda K, Shibata A, Matsuda T, Sobue T, et al. Incidence of myelodysplastic syndrome in Japan. J Epidemiol 2014;24:469−73.
[7] Awidi A, Magableh A, Taimeh Z, Ayyad H, Bsoul N, Tarawneh M. Primary myelodysplastic syndrome in Jordan: a single-centre experience. Med Princ Pract 2009;18:351−5.
[8] Demirkan F, Alacacioglu I, Piskin O, Ozsan HG, Akinci B, Ozcan AM, et al. The clinical, haematological and morphological profile of patients with myelodysplastic syndromes: A single institution experience from Turkey. Leuk Lymphoma 2007;48:1372−8.
[9] Al-Ghazaly J, Al-Selwi AH, Abdullah M, Al-Jahafi AK, Al-Dubai W, Al-Hashdi A. Pattern of haematological diseases diagnosed by bone marrow examination in Yemen: a developing country experience. Clin Lab Haematol 2006;28:376−81.
[10] Elnahass Y, Youssif L. Cytogenetic features in primary myelodysplastic syndrome Egyptian patients. J Adv Res 2018;10:77−83.
[11] International Standing Committee on Human Cytogenetic Nomenclature, Shaffer LG, McGowan-Jordan J, Schmid M, editors. ISCN 2013: an international system for human cytogenetic nomenclature (2013). Basel: Karger; 2013.
[12] Paydas S. Young age MDS: Differences between Western and Eastern countries. Leuk Res 2006;30:362.
[13] Greenberg PL, Stone RM, Al-Kali A, Barta SK, Bejar R, Bennett JM, et al. Myelodysplastic syndromes, version 2.2017, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 2017;15:60−87.
[14] Goasguen JE, Bennett JM, Bain BJ, Brunning R, Vallespi MT, Tomonaga M, et al. Proposal for refining the definition of dysgranulopoiesis in acute myeloid leukemia and myelodysplastic syndromes. Leuk Res 2014;38:447−53.
[15] Miyazaki Y, Tuechler H, Sanz G, Schanz J, Garcia-Manero G, Solé F, et al. Differing clinical features between Japanese and Caucasian patients with myelodysplastic syndromes: Analysis from the International Working Group for Prognosis of MDS. Leuk Res 2018;73:51−7.
[16] Al-Seraihy A, Ayas M, Al-Nounou R, El-Solh H, Al-Ahmari A, Al-Jefri A, et al. Outcome of allogeneic stem cell transplantation with a conditioning regimen of busulfan, cyclophosphamide and low-dose etoposide for children with myelodysplastic syndrome. Hematol Oncol Stem Cell Ther 2011;4:121−5.