Comparison of the Revised 4Th (2016) and 5Th (2022) Editions of the World Health Organization (WHO) Classification in a Cohort of Patients with Lower-Risk Myelodysplastic Syndromes/Neoplasms (MDS) - a Glam Registry (REGLAM) Analysis

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INTRODUCTION

The 5th (2022) edition of the WHO Classification for MDS recognizes MDS patients into two groups: MDS with defining genetic abnormalities and MDS morphologically defined. Further, the revised International Prognostic Scoring system (IPSS-R) assigns MDS patients into one of prognostic groups with distinct survival probabilities. However, both the IPSS-R and the 2022 WHO classification were developed based on data largely generated from patients in the high-income countries. There are limited data of how these systems perform in patients from developing and middle-income countries (LMIC).

AIM

The primary objective of this study was to compare the performance of the two WHO classifications: the revised 4th (2016) and 5th (2022) editions in IPSS-R defined Lower-Risk MDS Cohort of patients from LMIC in the GLAM registry.

METHOD

- The Glam Registry enrolls patients from 16 Latin-American countries
- For this analysis, we selected Lower risk MDS (defined as IPSS <3.5)
- CMML and higher-Risk MDS were excluded
- The study was conducted in compliance with local regulations, and all subjects signed inform consents.
- Descriptive statistics, Sankey Diagram, Kaplan Meier methods and the Confidential Interval for the 5-year survival probability were used to report the results.
- Overall survival (OS) was measured from time of diagnosis to last contact or death, and progression-free survival (PFS) was measured from time of diagnosis to disease progression, progression to acute myeloid leukemia (AML), or death.

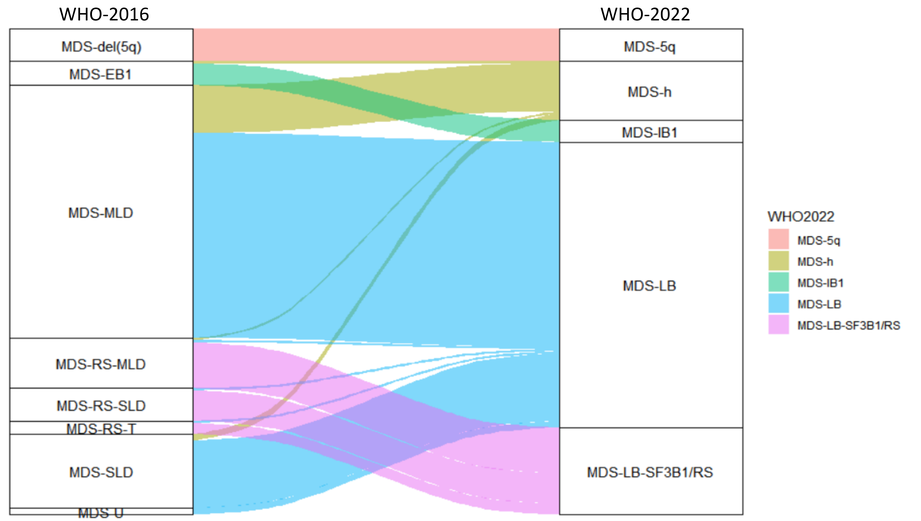
RESULTS

n = 223 LR-MDS patients

Therapy-related MDS: 7%

Baseline Characteristics, Demographics, and Survival Probabilities according to 2016 and 2022. WHO Classifications	
Age at diagnosis, median (range)	68.5 (16-94)
Male sex, n (%)	104 (46.6)
Non-Hispanic White, n (%)	89 (71.2)
Hemoglobin (gm/dl), median (range)	9.8 (3.7-16.4)
WBC count (x10°/L), median (range)	3.8 (0.1-22)
ANC (x10°/L), median (range)	3.4 (0.05-90)
Platelet count (×10°/L), median (range)	149 (2-900)
Peripheral blast (%), median (range)	0 (0-10)
Bone marrow blast (%), median (range)	1 (0-8)
Transfusion dependent, n (%)	61 (44.2)
SF3B1 Mutation	6/27 (22.2)
Median Overall Survival (years)	6.4 (95%CI 4.4-NA)
Median Leukemia Free Survival (years)	5.5 (95%CI 4.4-NA)

Shifts in classification of patients between the 2016 and 2022 version



Sankey diagram showing IPSS-R Lower-Risk MDS patients´ transition in categorization according to 2016 and 2022 WHO Classifications

WHO-2016	OS (years)	LFS (years)
MDS-RS-SLD	8.4 (0.8-NA)	8.4 (0.8-NA)
MDS-RS-MLD	4.4 (1.8-NA)	4.4 (1.8-NA)
MDS-RS-T	2.5 (0.3-NA)	2.5 (0.3-NA)
MDS-del(5q)	4.1 (2.8-NA)	4.1 (1.3-NA)
MDS-SLD	Not reached	Not reached
MDS-MLD	6.4 (3.8-NA)	6.4 (3.8-NA)
MDS-EB1	4.4 (1.0-NA)	3.9 (0.7-NA)
MDS-U	Non-Calculated	Non-Calculated
WHO-2022	**OS (years)**	**LFS (years)**
MDS-SF3B1/RS	5.5 (2.8-NA)	5.5 (2.8-NA)
MDS-del(5q)	4.1 (2.8-NA)	4.1 (1.4-NA)
MDS-LB	5.2 (3.8-NA)	5.2 (3.5-NA)
MDS-h	Not-reached	Not reached
MDS-IB1	4.4 (1.0-NA)	2.7 (0.7-NA)

- There were no cases of **biTP53-mutation** among the 12.1% of patients who had testing for TP53.
- Three patients were **re-classified** from **MDS-RS-MLD** (WHO-2016) to **MDS-LB** (WHO-2022) because SF3B1 mutation was associated with complex karyotype, del(5q), del(7q) and/or TP53 monoallelic.
- Four patients with **MDS-U** (WHO-2016) were **re-classified** to **MDS-LB** (WHO-2022).

- **MDS-LB** category (WHO-2022) was a large and a very heterogeneous group with an OS and LFS of 5.2 years.

WHO-2016		WHO-2022	
MDS-RS-SLD	15 (6.72%)	MDS-LB-SF3B1-RS	40 (17.9%)
MDS-RS-MLD	23 (10.3%)	MDS-biTP53	0 (0%)
MDS-RS-T	6 (2.7%)	NA	NA
MDS-del(5q)	15 (6.7%)	MDS-del(5q)	15 (6.7%)
MDS-SLD	34 (15.2%)	MDS-LB	131 (58.7%)
MDS-MLD	116 (52%)	MDS-h	27 (12.1%)
MDS-EB1	11 (4.9%)	MDS-IB1	10 (4.4%)
MDS-EB2	0 (0%)	MDS-IB2	0 (0%)
MDS-U	3 (0.66%)	MDS-f	0 (0%)

WHO-2016	5-year OS	5-year LFS
MDS-SLD	62.5%	62.5%
MDS-MLD	54.6%	53.6%

CONCLUSIONS

- Our study, to our knowledge, provides one of the first, if not the first, **datasets from LMIC** to describe **characteristics of IPSS-R lower-risk MDS pts** and their **re-classification** and corresponding **survival** according to the WHO 2016 and 2022 classifications.
- **Limited availability of molecular analysis** in real-life settings (e.g., *TP53* mutations) **highlights** some of the challenges of using the 2022 WHO classification (as well as IPSS-M) in LMIC.
- Understanding the **epidemiology of MDS** pts in LMIC is important especially as some of **the newly approved agents** for lower risk MDS are starting to be used in these countries.

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