**Severity of Covid-19 Clinical Outcomes and Mortality in Multiple Myeloma Patients over Year 1 of the Pandemic**

In the first weeks of the Covid-19 pandemic when healthcare systems in many areas were overstretched, we documented that hospital mortality in multiple myeloma (MM) patients infected by Sars-Cov-2 was 50% higher than in age matched Covid-19 patients without cancer.   
In the following months, the pressure on healthcare systems in Spain continued although it did not reach the extreme levels of the first weeks of the pandemic. In this study, we proposed to determine if the severity of Covid-19 outcomes in MM patients has changed over the first year of the pandemic.

**Patients and methods**

The Spanish MM Collaborative Group (Pethema-GEM) conducted a survey at national level on plasma cell disorder patients infected by SARS-Cov-2 between March 2020 and February 2021. Sixty-six (69%) out of 96 contacted healthcare centers, from all 17 regions in Spain, reported 502 patients. Data on Covid-19 acute and post-acute phase outcomes (hospitalization, oxygen requirements, severity of symptoms and mortality) were reported first in May 2020 (Martinez-Lopez et al, BCJ 2021) and updated in February 2021. In this study, we compared outcome occurrence between two study periods: P1, a period of extreme stress for the healthcare system in Spain, from March to mid-June 2020; and a second period, P2, up to mid-February 2021 with a sustained but lower burden on the national health care system.

**Results**

Among the 451 patients with plasma cell disorders and a Sars-Cov-2 infection documented with an rRT-PCR positive test, 377 (84%) were MM patients, 15 SMM (3%), 40 MGUS (9%) and 19 amyloidosis (4%). The number of MM weekly reported cases was 57% (95%CI, 48-65) lower in P2 (188 cases in 35 weeks) compared to P1 (189 cases in 15 weeks), p<0.001. The mean (SD) age and the proportion of men did not differ between P1 and P2, respectively 69.8 (10.9) vs 68.6 (11.0) years, p=0.6, and 53.3% vs 59.6%, p=0.2.

MM patients with active or progressive disease at time of Covid-19 diagnosis were 24% in P1 and 34% in P2, p=0.05; patients on active treatment were more frequent in P1, 89%, than in P2, 79%, p=0.01. MM treatment was withheld in 78% and 82% of patients, p=0.4.

Covid-19 treatment changed over time: MM inpatients received more remdesivir and corticoids in the second period (3% vs 31% p<0.001, and 49% vs 73%, p<0.001, respectively).

In P1, 90% of the reported MM patients were hospitalized compared to 71% in P2, p<0.001. Thirty-one and 41% of patients did not require oxygen support during P1 and P2, respectively; non-invasive ventilation in 19% and 14%, and mechanical ventilation in 7% and 8%, p=0.12. Overall, acute clinical Covid-19 severity was reduced from P1 to P2: 75% to 51%, p<0.001: moderate/severe pneumonia was reduced from 68% to 36%, p<0.001 but severe distress syndrome increased from 7% to 15%, p=0.03. However, mortality in all reported patients was 30.7% in P1 vs 26.1% in P2, p=0.3; and no differences in mortality were observed in hospitalized patients, 32.2% in P1 and 35.3% in P2, p=0.6.

We performed a multivariable adjustment with the predictors identified in our previous study (BCJ 2021) and confirmed that inpatient mortality was similar in both study periods, odds ratio (OR) 0.99 (95%CI 0.59-1.66).

Independently of the study period, an increased mortality was observed in men (OR 1.81, 1.08-3.05), patients over 65 (OR 2.40, 1.33-4.36), and patients with active or progressive disease (OR 2.12, 1.24-3.62). The severity of Covid-19 clinical outcomes –besides mortality, was associated with increased age but not with active or progressive disease.

**Conclusions**

Although COVID-19 clinical severity has decreased over the first year of the pandemic in multiple myeloma patients, mortality remains high with no change between the initial weeks of the pandemic and the following months. Prevention and vaccination strategies should be strengthened in this vulnerable population, particularly in patients with active or progressive disease at time of Covid-19 diagnosis.