

EMERGENCY MYELOPOIESIS, CLINICAL CHARACTERISTICS AND PRE-CONDITIONS AS PREDICTIVE OUTCOME SIGNATURES FOR SEVERE COVID-19 YOUNG PATIENTS IN MEXICO

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IUIS-FAIA-SANTHE-ISZ IMMUNO-ZAMBIA 2022

ABSTRACT

More than a half of COVID-19 reported deaths in Mexico and 63% hospitalizations are register in adults younger than 65 years old (yo), with an important rise at ages 40-50. Of importance, 67% of individuals who died to COVID-19 had at least one preexisting chronic disease and almost 40% had two or more. Mexico, as many countries in Latin America, has a large burden of pre-existing metabolic diseases, leading overweight/obesity (71.3%) and diabetes (15.7%).

We evaluate the contribution of clinical characteristics and pre-conditions to emergency hematopoiesis and immune response, in a prospective cohort with 245 hospitalized COVID-19 patients, from October, 2020 - September, 2021.

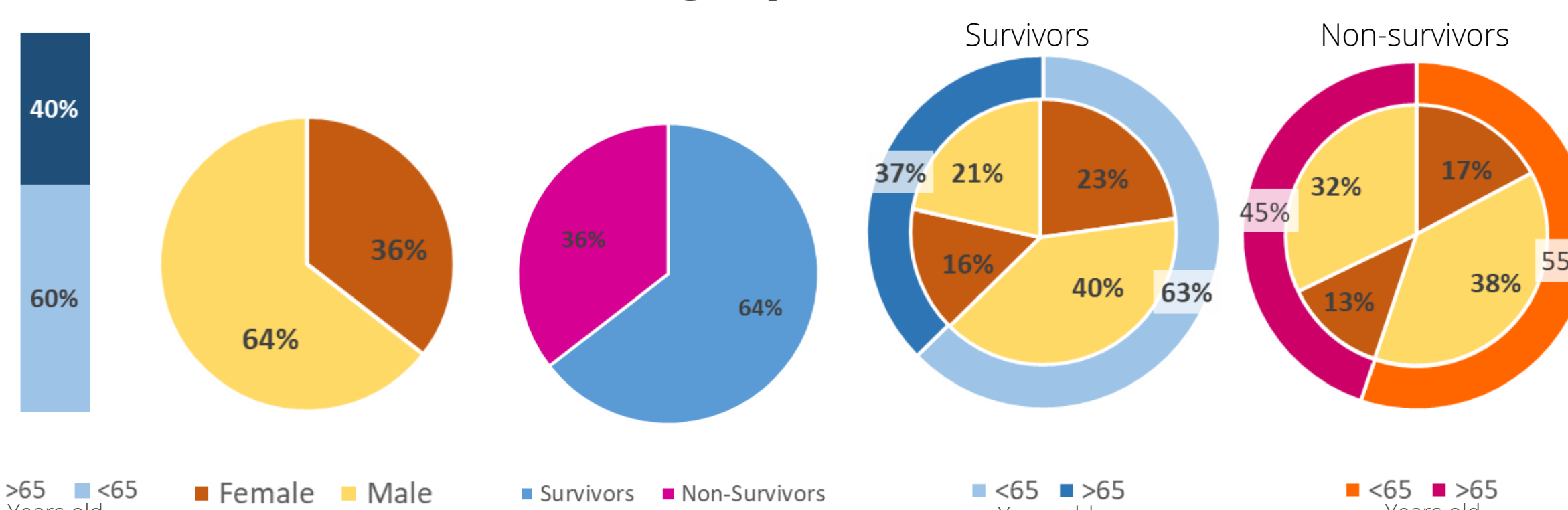
Fatal outcomes were marked by an inflammatory landscape, leading to imbalanced emergency myelopoiesis.

AIMS

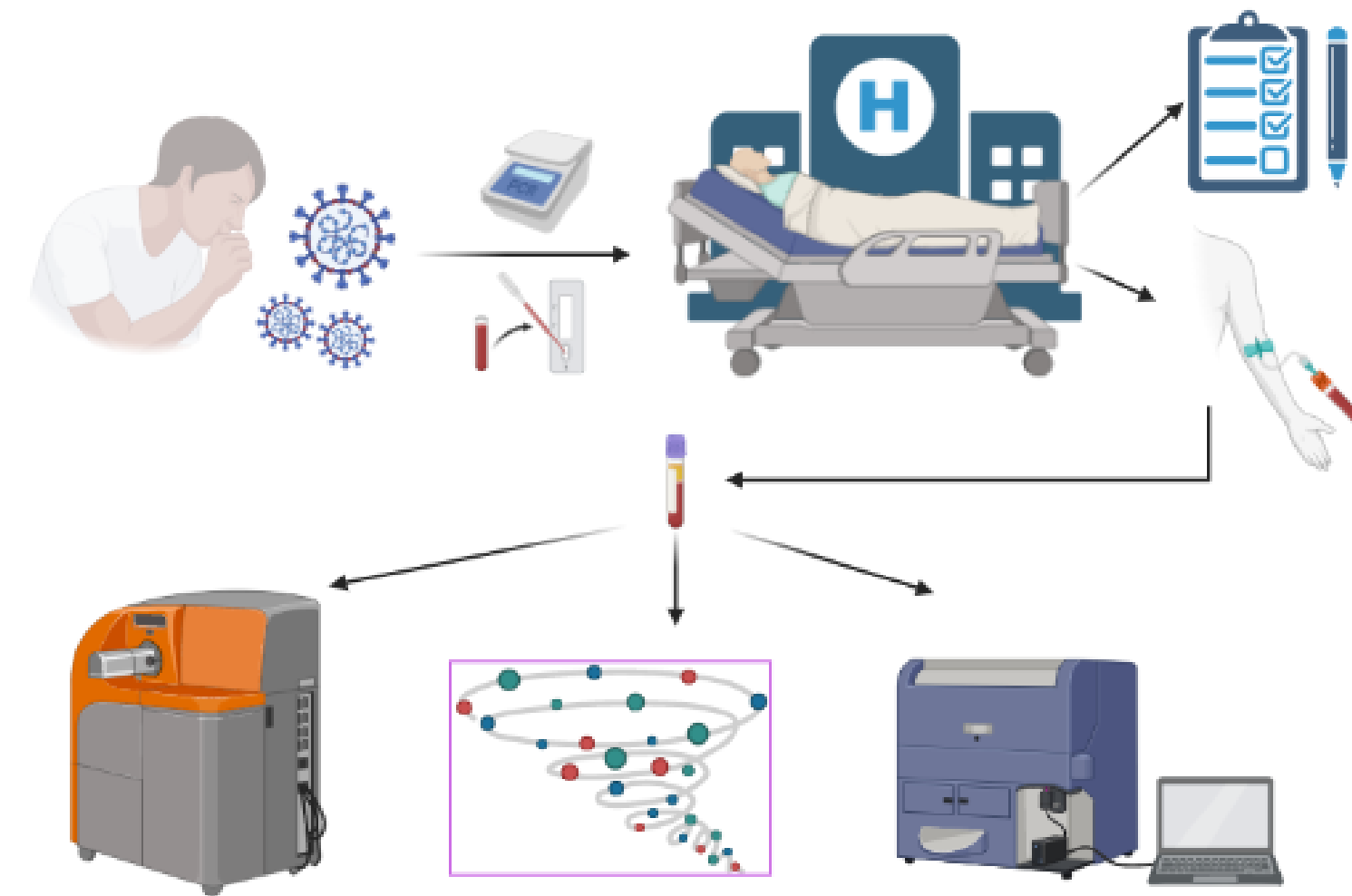
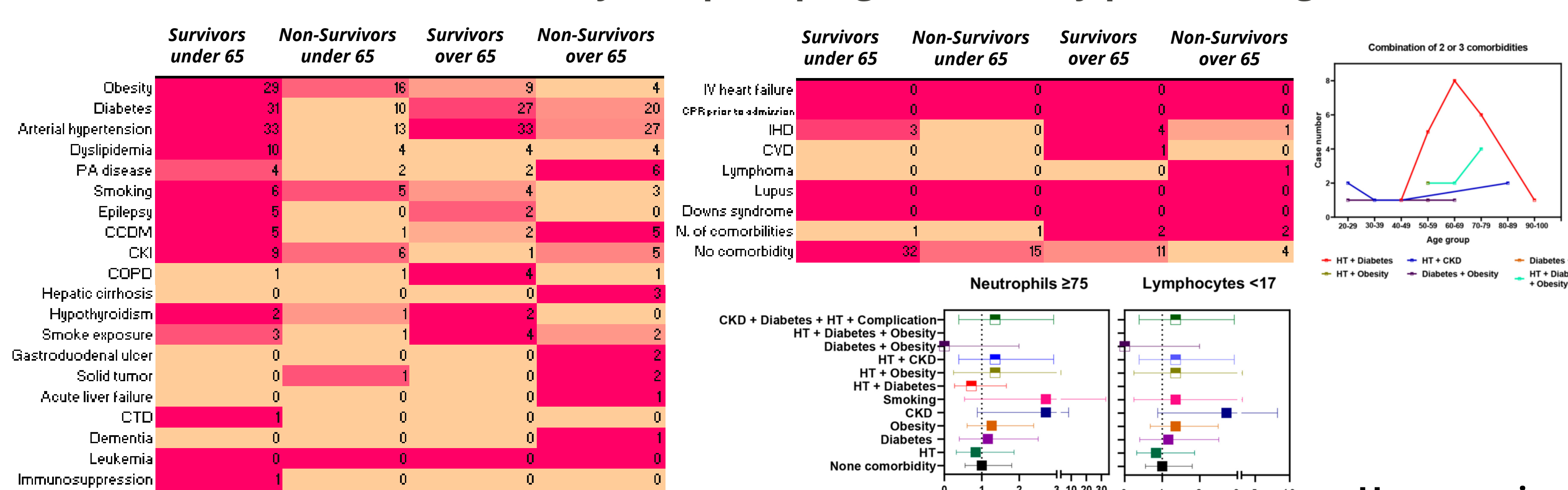
Generate a comprehensive understanding of the COVID-19 clinical spectrum in Mexico for crucial intervention to prevent the evolution towards severe disease.

RESULTS

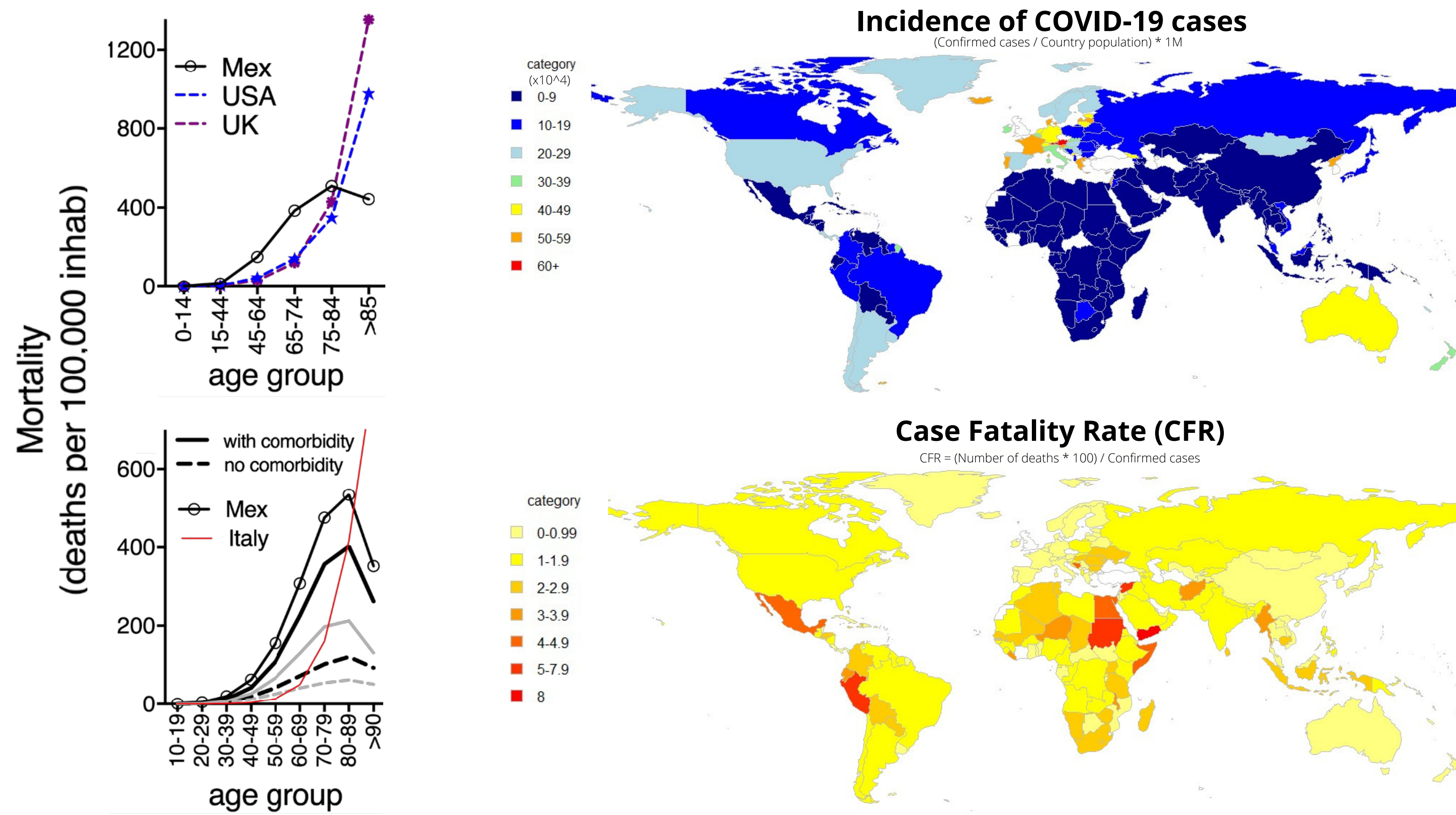
Atlixco cohort demographics and outcomes



Increase of COVID-19 fatality and poor prognosis risk by pre-existing conditions

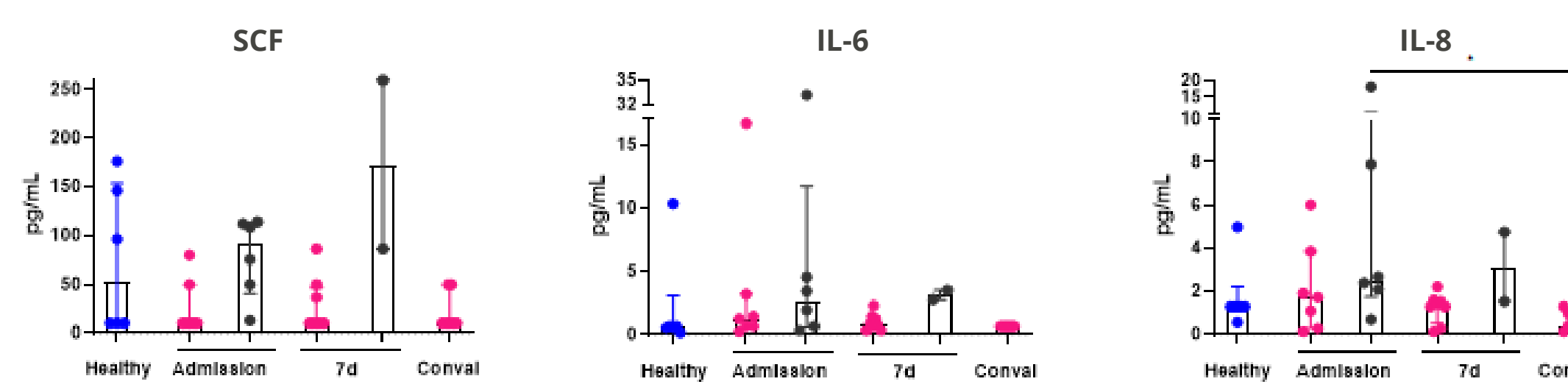


Mexico is one of the countries with the highest excess of mortality due to COVID-19 and pre-existing metabolic conditions of the population, which makes it challenging to resolve acute infections that largely depend on the prompt response of a functional hematopoietic system. The reduction of fatality rates in vulnerable regions of the world requires a comprehensive understanding of the relationship between the development of severe forms of COVID-19 and comorbidities. Male sex, older age, obesity, diabetes, and chronic kidney diseases have been highlighted as important risk factors of COVID-19 poor outcomes worldwide. Previous studies focusing on the association between metabolic diseases with severe COVID-19 on admission have underscored the urgent need for stratification profiles for vulnerable populations in Mexico, as about 74% of individuals who died of COVID-19 had at least one preexisting chronic disease, and the relative risk of COVID-19 death (RRd) contributed by having any comorbidity in Mexicans at different ages, has shown that RR of pre-existing disease decreased sharply with age. Importantly, middle aged-adults in Mexico are the population with higher CFR and mortality compared to very high-income countries, with more than half of reported deaths occurring in this group.

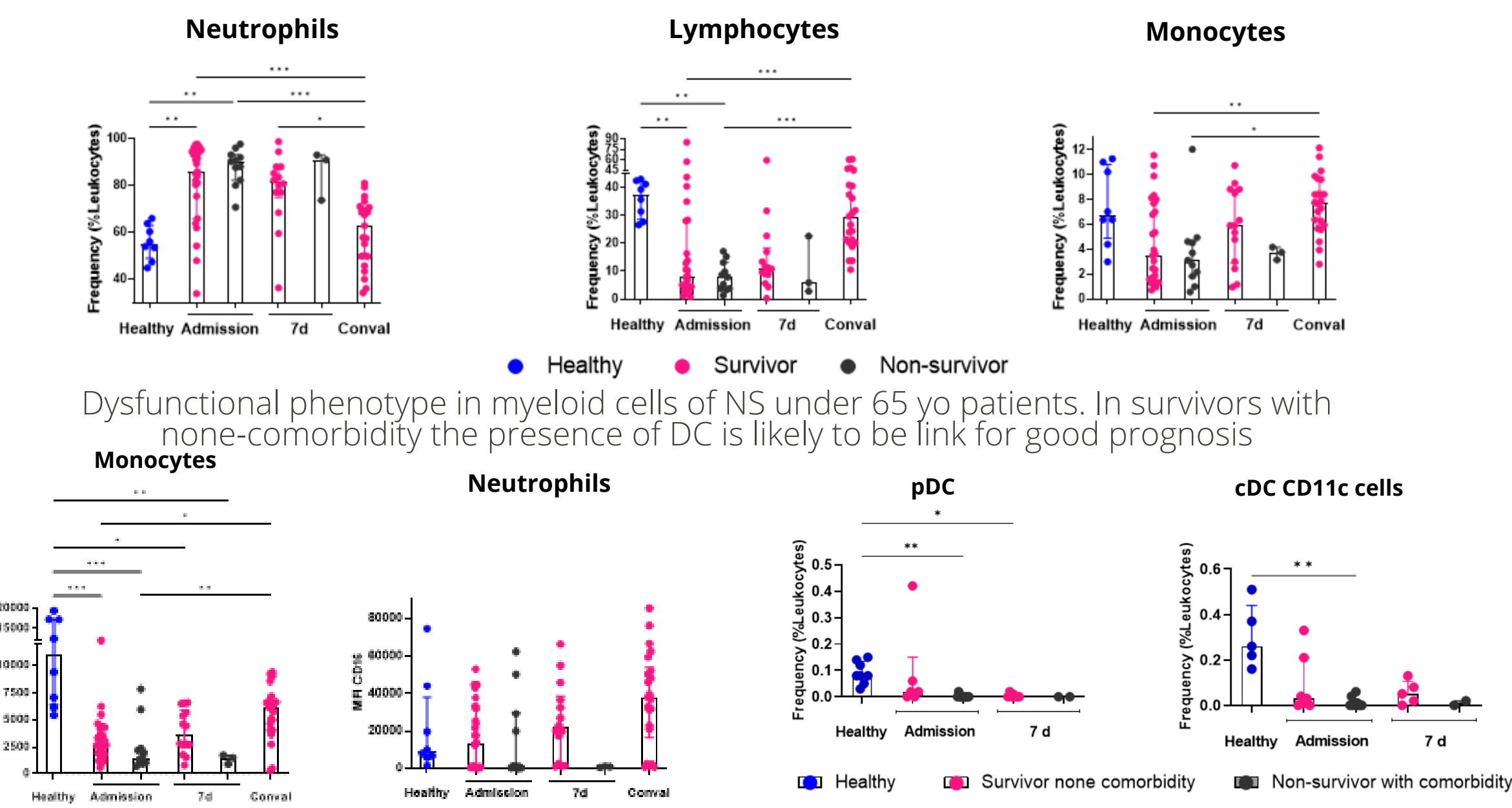


Obtained from: Domínguez-Ramírez L, et al; 2020

Inflammatory profile in non-survivor middle-aged patients with important immunophenotype changes

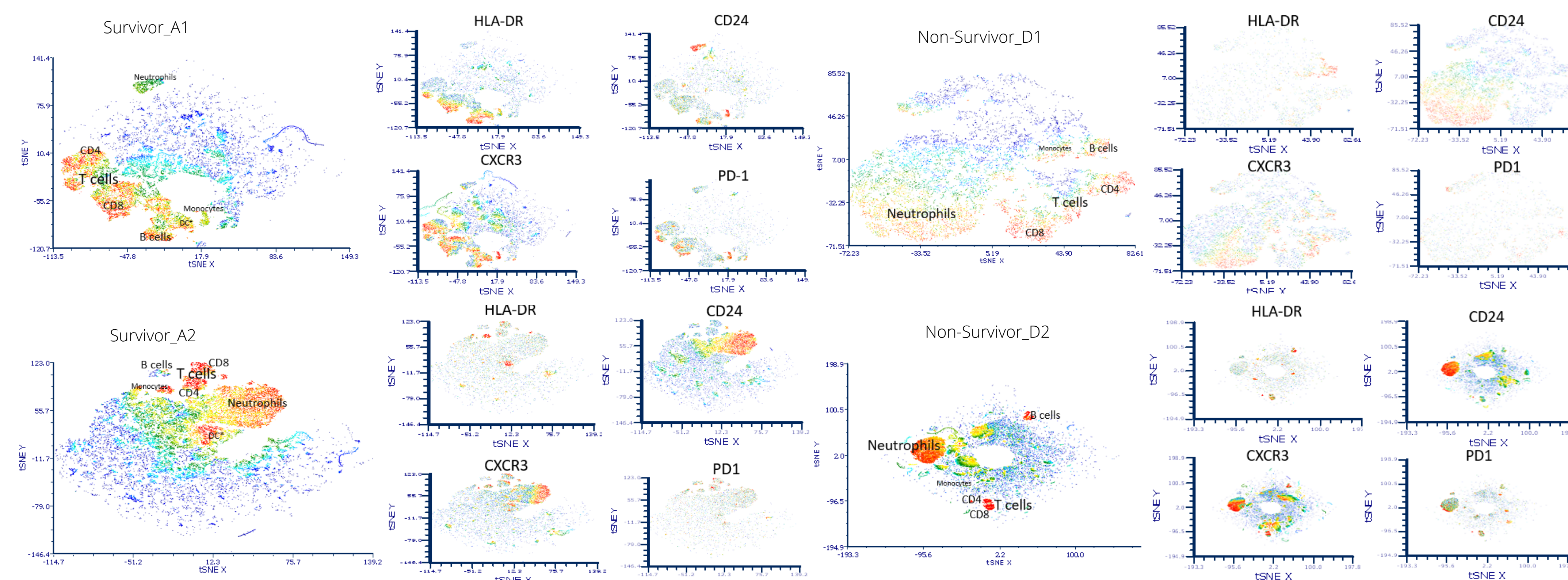


Myeloid emergency hematopoiesis is present in non-survivor middle-aged patients with important immunophenotype changes



Dysfunctional phenotype in myeloid cells of NS under 65 yo patients. In survivors with none-comorbidity the presence of DC is likely to be link for good prognosis

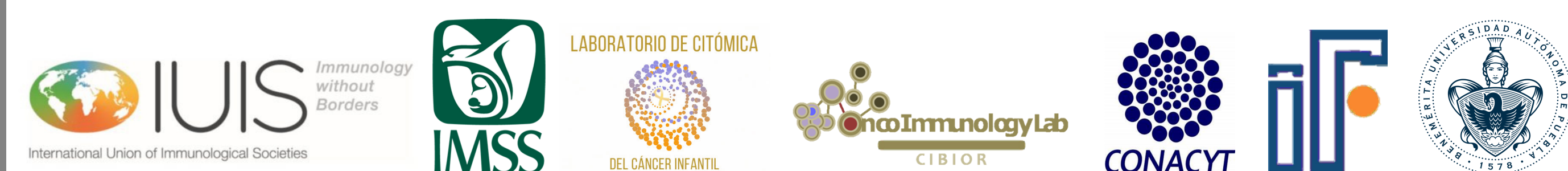
Unsupervised clustering analysis of mass cytometry data reveals neutrophils related to severe COVID-19 and co-expression of CXCR3



Chronic comorbidities are higher in younger populations. For older populations, age is the most important RR, while in patients younger than 65 yo the presence of more than 1 comorbidity increases importantly the RR, and also in combination with some hematological values

Acknowledgments

GZH and RRR acknowledge the scholarship provided by CONACYT. The authors acknowledge the Oncoimmunology and Cytomics Lab members for critical assistance, and the professional staff from COVID-19 reference hospitals at IMSS. To the Benemérita Universidad Autónoma de Puebla and remarkably to the IUIS who provided the scholarship for IMMUNO-Zambia course



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CONCLUSION

Comorbidities increased the development of imbalanced myeloid phenotype, rendering middle-aged individuals unable to effectively control SARS-CoV-2. Chronic comorbidities are a serious problem in Latin America, and especially in Mexico, this provides a pro-inflammatory microenvironment prompt to evolve into severe COVID-19 or fatal outcomes when the infection is established. The identification of pre-existing health conditions in combination with cell populations can help to create predictive signatures and targets against COVID-19.