REGULAR ARTICLE

Hispanic Ethnicity and Social Determinants of Health: Harnessing Data from The Pulmonary Hypertension Association Registry

Roberto J. Bernardo, MD, MS
Division of Pulmonary, Critical Care and Sleep Medicine
University of Oklahoma Health Sciences Center
Oklahoma City, OK

Vinicio A. de Jesus Perez, MD
Division of Pulmonary and Critical Care Medicine
Stanford University School of Medicine
Stanford, CA
Vera Moulton Wall Center for Pulmonary Disease at Stanford University
Stanford, CA

Pulmonary arterial hypertension (PAH) is a chronic, progressive, and debilitating disease associated with increased cardiopulmonary morbidity and mortality. Current knowledge is derived from registries and landmark clinical trials, although concern exists that minorities are underrepresented in these datasets, and it remains unknown if there are intrinsic differences in minorities and disadvantaged groups. The Pulmonary Hypertension Association Registry offers a unique opportunity for the understanding of the unique social background of minorities in the United States because it routinely collects information related to socioeconomic factors such as annual income and health care insurance. Furthermore, representation of Hispanic patients may be slightly higher than in other US-based registries.

In this review, we discuss the interplay between biologic, socioeconomic, and racial or ethnic factors in PAH, with special emphasis on the Hispanic population. We describe the unique socioeconomic profile of Hispanic individuals and propose next steps to improve representation and fight inequality for Hispanic patients with PAH.

INTRODUCTION

Pulmonary arterial hypertension (PAH) is a progressive pulmonary vascular disorder, characterized by progressive remodeling and narrowing of the pulmonary arterial tree,[1] resulting in increased right ventricular (RV) wall stress, abnormal RV mechanics, and if left untreated, right heart failure and death.[2,3] Despite significant progress in the understanding of the disease biology, delays in disease recognition and diagnosis are common, and most patients present at advanced stages. As such, emphasis should be on prompt recognition of the disease and associated factors that could be associated with higher risk of disease progression.[4]

Factors associated with progression of disease include age, severity of symptoms, PAH subtype, exercise capacity, metrics of RV function, hemodynamics, and biomarkers such as natriuretic peptides.[5–7] Current clinical models of PAH progression are derived from large randomized clinical trials (RTCs) and registries; however, concern exists that minorities and Black, Indigenous, and people of color (BIPOC) are underrepresented in these registries and RCTs.[8–10]

PULMONARY HYPERTENSION IN MINORITIES

Noticeable underrepresentation of minorities such as Hispanics in most PAH RCTs and registries exists (Figures 1A and 1B). This is an area of concern because most prognostic models in PAH are derived from these datasets, and patients of diverse backgrounds get treated from data that may not represent the same diversity. Accurate racial and ethnic representation is important to determine the generalizability of treatment approaches and outcomes in PAH.[10]

For instance, in the landmark SERAPHIN trial, only 14.7% of participants were of Hispanic ethnicity compared with 54.5% of White participants[11] (Figure 1A). Moreover, in the REVEAL registry (Registry to Evaluate Early and Long-term PAH Disease Management), the proportion of Hispanics was 8.9%, while the expected proportion of Hispanics should have been close to 11.5%, based on US census estimates (Figure 1B). Similarly, the proportion of Asian or Pacific Islander participants was 3.3% in comparison with an expected proportion of 6.1%.[9]

As such, the American Thoracic Society statement on health disparities in patients with PAH emphasized that PAH registries should be organized to reliably capture information related to race or ethnicity and socioeconomic factors and that socioeconomic factors should be addressed since they may allow identification of patients at the greatest risk for treatment noncompliance.[8]

Then the need to further describe the interplay between the biologic,

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Correspondence: Roberto-Bernardo@ouhsc.edu
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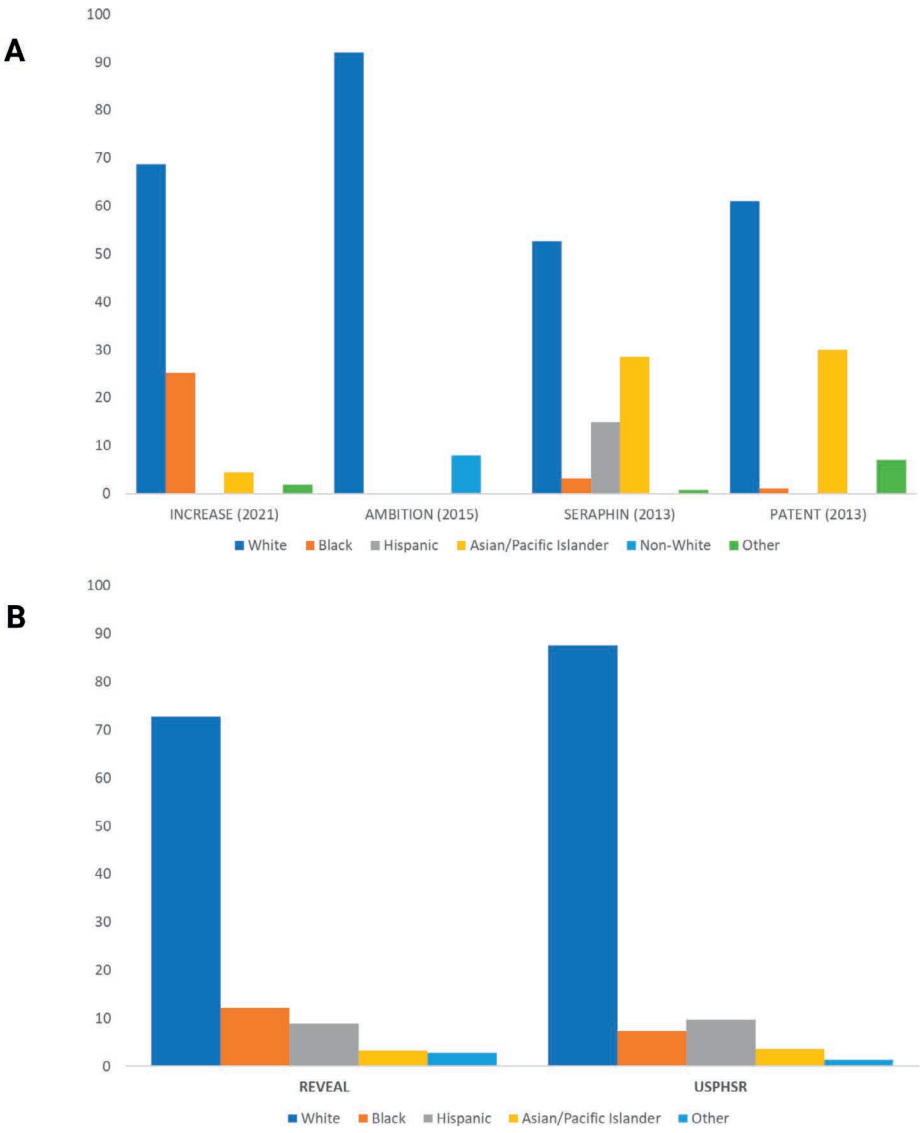

Figure 1: Representation of minorities and BIPOC in PAH clinical trials and registries. (**A**) Data in PAH clinical trials and (**B**) data in US-based registries. BIPOC = Black, Indigenous, and people of color; PAH = pulmonary arterial hypertension; REVEAL = Registry to Evaluate Early and Long-term PAH Disease Management; USPHSR = United States Pulmonary Hypertension Scientific Registry.

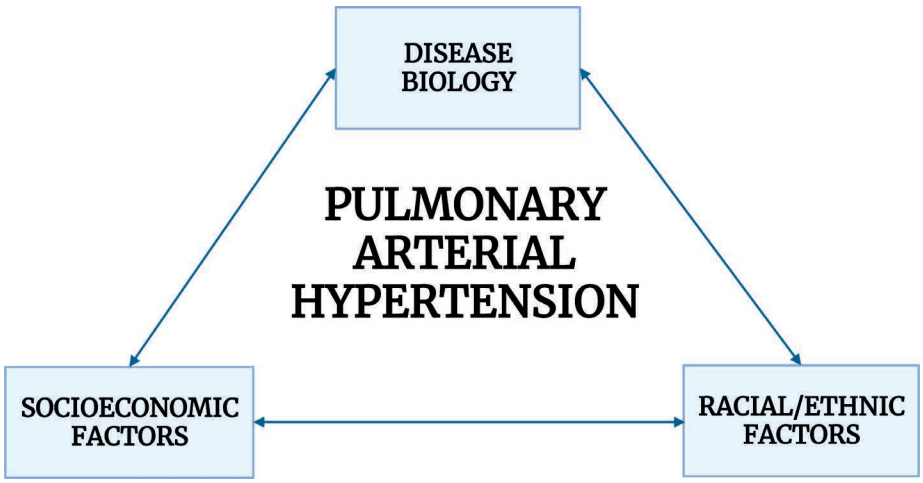

Figure 2: Interplay between biologic, socioeconomic, and racial/ethnic factors in PAH. PAH = pulmonary arterial hypertension.

socioeconomic, and racial or ethnic factors of the disease becomes evident (Figure 2).

PULMONARY HYPERTENSION AND SOCIOECONOMIC FACTORS

Socioeconomic status (SES) refers to an individual's social and economic standing and is a measure of social or economic position or ranking in a social group.[12] SES is a composite of several measures including income, education, occupation, residence, and housing, among others.[8] Unfortunately, socioeconomic factors are not routinely collected in most PAH registries, such as REVEAL.

Authors of a few studies have addressed the significance of SES in PAH. Wu et al[13] found that SES was an independent factor associated with impaired clinical outcomes in a cohort of patients with PAH in China. SES was measured as a composite metric of education, annual income, occupation, and medical reimbursement rate. Individuals in the lowest tertile of SES had increased hazard ratios for all-cause mortality, after adjusting for age, sex, World Health Organization (WHO) functional class, pulmonary vascular resistance, and PAH treatment. Talwar et al[14] found that patients with the lowest annual income had higher WHO functional class on initial presentation in a large US medical system database. Median annual income was estimated based on zip codes of study participants. On the other hand, authors of a relatively recent study from Scotland did not find an association between social deprivation and either severity of disease (WHO functional class) or all-cause mortality.[15] In this study, the investigators used geographical data zones to infer SES.

Social determinants of health (SDOH) refer to conditions in which individuals are born, grow, live, work, and age[16] and are implicated in health inequalities and poor conditions of daily life, which disproportionately affect certain groups such as minorities and BIPOC.[17,18] We will discuss SDOH in PAH in more detail later in this review.

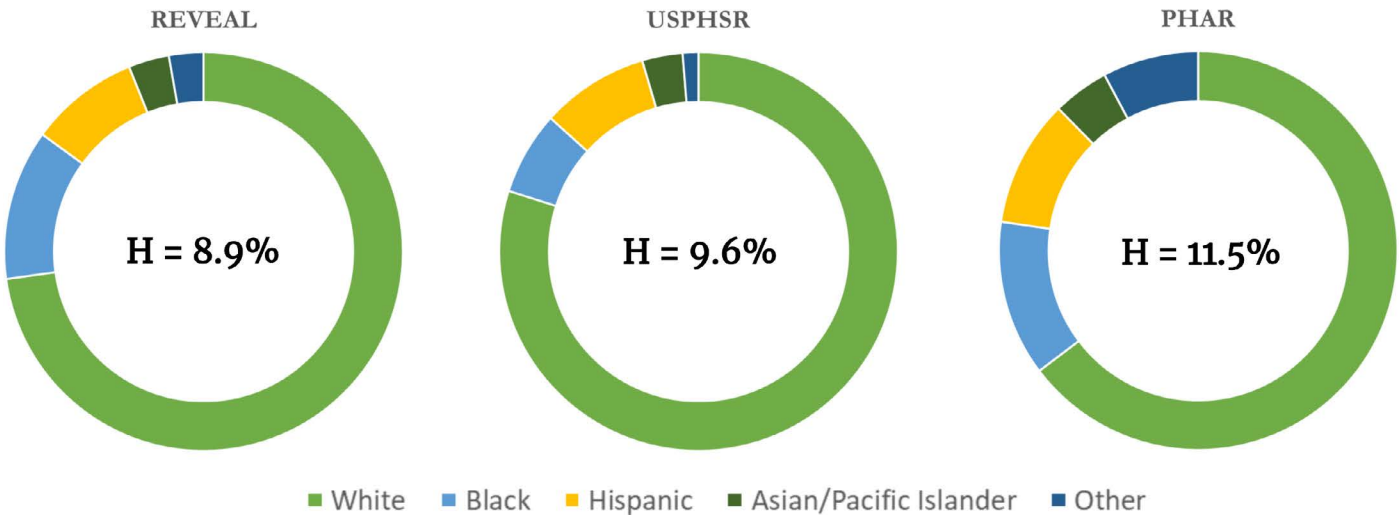

Figure 3: Representation of Hispanic patients in PAH registries. H = Hispanic patients; PAH = pulmonary arterial hypertension; PHAR = Pulmonary Hypertension Association Registry; REVEAL = Registry to Evaluate Early and Long-term PAH Disease Management; USPHSR = United States Pulmonary Hypertension Scientific Registry.

PULMONARY HYPERTENSION AND RACE OR ETHNICITY

Race is defined as "major living subspecies of man differentiated by genetic and physical characteristics," while ethnicity involves factors such as cultural heritage and sociocultural background.[9] Ethnicity is a concept closely related to SDOH: It refers both to the social factors promoting or undermining the health of individuals and the social processes underlying an unequal distribution of these factors, leading to differences in access to health care services and ultimately health care disparities.[19,20] We prefer to use the term ethnicity in lieu of race to encompass both genetic and cultural attributes.[21]

Racial or ethnic factors have been an area of interest in PAH, and most studies have been performed with Black and Hispanic patients.[9,22,23] Regarding Black patients with PAH, a higher frequency of connective tissue disease (i.e., scleroderma)[9] as well as a different response pattern to endothelin-receptor antagonists has been reported.[24] No convincing evidence of differences in survival have been found.[25] We will focus most of our discussion on the Hispanic population.

In general terms, Hispanic patients with PAH tend to be younger and have a higher frequency of congenital heart disease and portopulmonary hypertension.[8,9] Authors of studies evaluating clinical outcomes in Hispanic patients with PAH have shown differing results. Karnes et al[26] used data from the PAH Biobank and found that Hispanic patients with idiopathic or hereditary PAH may have slightly better survival than non-Hispanic Whites, after adjusting for age, sex, pulmonary vascular resistance, and use of prostacyclin analogues (heart rate [HR] = 0.46, 95% confidence interval [CI] = 0.21–0.99). These findings were not replicated on a study by Medrek et al[25] using the REVEAL dataset, where no association between Hispanic ethnicity and survival was found, after adjusting for age and PAH etiology (HR = 0.97, 95% CI = 0.76–1.24).

It is important to note that neither the PAH Biobank nor REVEAL routinely collect socioeconomic metrics: The authors of these studies could not account for differences in SES or SDOH. As others have previously emphasized, studying the association between race or ethnicity and health care outcomes without assessing the impact of socioeconomic factors offers an incomplete picture of the problem.[27–29]

THE PULMONARY HYPERTENSION ASSOCIATION REGISTRY

An important mechanism of health inequality in PAH is the lack of inclusivity in registries and RCTs.[10] Not only is there underrepresentation of minorities and BIPOC in most datasets, but most US registries do not routinely collect socioeconomic metrics, except for the Pulmonary Hypertension Association Registry (PHAR). PHAR is a multicenter US-based registry of patients treated at different pulmonary hypertension care centers. PHAR prospectively collects data from adults and children with PAH and chronic thromboembolic pulmonary hypertension.[30,31]

PHAR is a particularly unique dataset because metrics of SDOH such as income, education level, occupation, and health insurance are routinely collected. Furthermore, the representation of Hispanics in PHAR is slightly higher than REVEAL and other registries (Figure 3). As such, PHAR allows for the assessment of significance of SDOH in PAH, as previously reported.[32]

SDOH IN HISPANICS: DATA FROM PHAR

As mentioned above, authors of prior studies on clinical outcomes in Hispanic individuals with PAH had shown differing results and had not been able to assess the significance of socioeconomic metrics. Using data from PHAR, we recently performed a comprehensive characterization of Hispanic patients with PAH not only in terms of demographic and clinical factors but their social and economic profiles.[33] Hispanic patients were younger, had higher frequency of congenital heart disease, had higher pulmonary pressures and pulmonary vascular resistance, but had no major

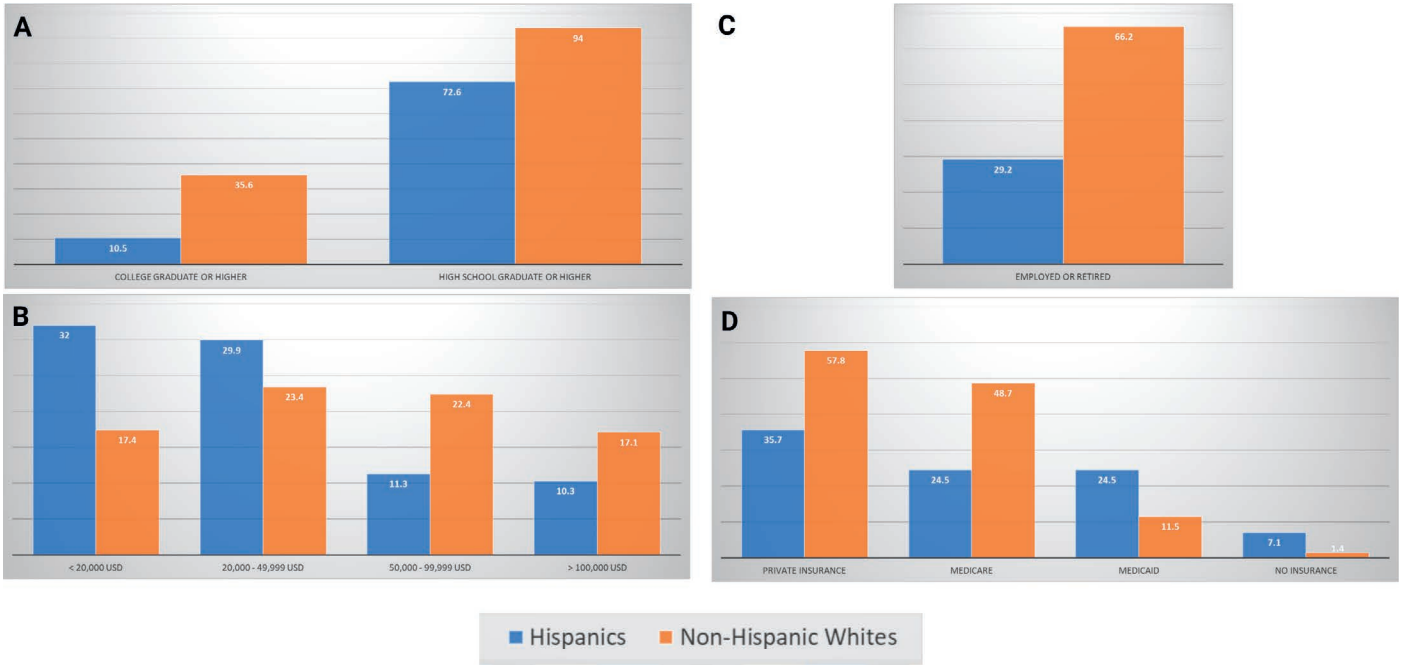

Figure 4: Social determinants of health in Hispanic and non-Hispanic White patients with PAH. Comparison of (**A**) education level, (**B**) total annual income, (**C**) occupation, and (**D**) health care insurance. Adapted from Bernardo et al.[33] PAH = pulmonary arterial hypertension.

differences in WHO functional class, exercise capacity, natriuretic peptides, or PAH therapy.

Hispanic patients had a disadvantageous socioeconomic profile as compared with non-Hispanic Whites. Hispanics had lower education level, had lower annual income, were less likely to be employed or retired, and were less likely to have access to Medicare or commercial insurance (Figures 4A–4D). For instance, up to a third of Hispanics were living with an annual income lower than $20000 per year as compared with 17.4% of non-Hispanic Whites. Only 29.2% of Hispanics were either employed or retired compared with 66.2% of non-Hispanic Whites.

No differences existed in transplant-free survival between Hispanics and non-Hispanic Whites, after adjusting for age, SDOH, and other covariates (hazard ratio = 0.76, 95% CI = 0.35–1.62; P = 0.474). However, while no differences in survival were found, Hispanic patients had a higher number of emergency room visits, with an incidence of 3.1 visits per person-years as compared with 2.1 in non-Hispanic Whites (incidence rate ratio = 1.452, 95% CI = 1.326–1.590). The total number of hospitalizations and the number of cumulative days in the hospital were also higher among Hispanics.

Despite having a similar severity of illness at baseline, a higher frequency of emergency visits and hospitalizations suggests that disease control was less optimal in Hispanics, which could be related to a disadvantageous SDOH profile. Lower-income patients face several challenges regarding PAH care, such as inability to afford the cost of medications or medical testing.[10,33]

IMPROVING REPRESENTATION OF MINORITIES WITH PAH

As described through this review, an important mechanism of health inequality and disparities in care in PAH is the lack of inclusivity in national registries and clinical trials.[10] Patient registries have historically lacked adequate representation of minorities and BIPOC, limiting our capacity to determine differences in clinical phenotypes and implementation of therapies.[8] We agree with the statement from the American Thoracic Society,[8] and 2 important messages are that (i) PAH registries must be organized to reliably capture information concerning race/ethnicity and SES of patients, and (ii) SES should be included in the risk stratification to help identify patients with PAH who may be at greatest risk for noncompliance.

We agree with Goel et al[10] on their proposal of future next steps against inequality in PAH, such as optimizing access to PAH centers (where RCTs are being conducted), identifying and addressing inherent biases in providers and patients regarding health literacy, financial burden, or nonadherence patterns, and eliminating language barriers for access to RCTs. The fights against inequality will require joint effort among providers, hospitals, health insurers, industry, patients' associations, and professional societies such as the Pulmonary Hypertension Association and government. It is time for action.

CONCLUSIONS

Noticeable underrepresentation of minorities such as Hispanics in most PAH registries and RCTs exists. While clinical outcomes in PAH may not be due to race per se, noticeable differences exist in the access to specialized care for minority and BIPOC patients. Lower-income patients face several challenges regarding PAH care, and it is pivotal to assess the significance of socioeconomic metrics and SDOH in patients with PAH. Finally, we believe that PAH registries must be organized to reliably capture

information concerning race/ethnicity and SES of patients, and PHAR is an important step forward in this goal.

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