



Addressing the impact of ethnicity on asthma care

Tunn Ren Tay^a, Jonathan Pham^b, and Mark Hew^{b,c}

Purpose of review

In asthma, there is an increasing focus on personalizing treatment by targeting treatable traits. Ethnicity has effects on many biological and behavioural traits, and so is an important consideration when personalizing asthma care. This review has particular relevance in light of current patterns of international migration, which are leading to unprecedented levels of ethnic heterogeneity in many geographic regions.

Recent findings

This review examines the effect of ethnicity on three key domains – biological traits, behavioural traits and health system behaviour. Ethnicity influences asthma biology by affecting biomarker reference ranges, response to drug therapy and asthma phenotypes. Ethnicity impacts behavioural traits through its effects on psychosocial well being, adherence and asthma self-management. Ethnic minorities are often disadvantaged with regards to healthcare access and healthcare interactions.

Summary

Concerted action is needed to address current issues around behavioural traits and healthcare behaviour, which are influenced by ethnicity. More research is required to understand the impact of ethnicity on asthma biology, especially the interplay between genetic and environmental influences on asthma, and the differential response to asthma therapies.

Keywords

personalized medicine, pharmacogenomics, phenotype, race, socioeconomic

INTRODUCTION

There is increasing emphasis in asthma management on personalizing therapy by targeting an individual's specific biological and behavioural traits [1]. Biological traits relate to pulmonary and extrapulmonary attributes, such as airway inflammation, airflow limitation and comorbidities, whereas behavioural traits include medication adherence and self-management. Ethnicity – encompassing an individual's genetic ancestry, geographic background and cultural tradition – influences both biological and behavioural traits, and is thus an important consideration when personalizing asthma care [2].

Many healthcare models are based on evidence from ethnically homogenous populations. Extrapolation of such evidence to other populations may be inappropriate, given the unprecedented level of ethnic heterogeneity now present in many geographic regions, driven by extensive international migration.

In this review, we first examine how ethnicity affects biological traits – focusing on inflammatory biomarker reference ranges, differential responses to medications, and asthma phenotypes. We next discuss behavioural traits – focusing on psychological well being, medication adherence and self-management skills. Finally, we explore the behaviour of

health systems towards ethnic minorities – focusing on healthcare access and healthcare interactions (Fig. 1). Table 1 provides a summary of the evidence presented in this review.

BIOLOGICAL TRAITS

Biomarker reference ranges

For patients with severe asthma, guidelines recommend measurement of biomarkers, such as fractional exhaled nitric oxide (FENO) and sputum eosinophil counts to identify type 2 inflammatory phenotypes [3]. Normal reference ranges are derived mainly from Caucasian populations, but there is

^aDepartment of Respiratory and Critical Care Medicine, Changi General Hospital, Singapore, ^bAllergy, Asthma & Clinical Immunology, The Alfred Hospital and ^cPublic Health & Preventive Medicine, Monash University, Melbourne, Victoria, Australia

Correspondence to Tunn Ren Tay, Department of Respiratory and Critical Care Medicine, Changi General Hospital, Singapore, 2 Simei Street 3, 529889 Singapore. Tel: +65 6788 8833; e-mail: tay.tunn.ren@singhealth.com.sg

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KEY POINTS

- Ethnicity influences biological and behavioural traits in asthma.
- Ethnic minorities face disparities in healthcare access and healthcare interactions.
- Ethnicity should be considered when personalizing asthma treatment.

now evidence to suggest that such ranges may vary by ethnicity.

In one systematic review, ethnicity affected FENO values in 10 of 12 studies reviewed, with higher mean FENO values in Chinese and Korean adults than in Caucasians [4[•]]. More than 5% of FENO values from healthy Chinese and Korean adults would have been misclassified in the inflammatory range if the American Thoracic Society (ATS)-recommended FENO cut-off of 50 ppb was applied [4[•]]. In another study, healthy black adults had higher FENO levels compared to whites – the 95th percentile of FENO for black individuals was 43.3 ppb but 32.4 ppb for white individuals [5]. Similarly, for sputum cell counts, the 90th percentile for sputum eosinophil count was 3.5% in healthy South Koreans [6], but the 95% percentile was 2.2% in healthy Caucasians [7,8].

Given the importance of biomarkers for phenotyping asthma and directing treatment, ethnic-specific reference ranges must be established. This may require validating preexisting cut-off values in a variety of populations, or pooling normative data from international sources to derive multiethnic reference ranges.

Response to therapy

As in other areas of medicine, ethnic differences in drug response to asthma medications have been reported, although precise mechanisms are not well understood.

Response to corticosteroids

Suppressing the activation of T lymphocytes from black patients with asthma required higher concentrations of dexamethasone than those from white patients [9]. Black children with severe asthma were less likely than white children to suppress FENO levels with intramuscular triamcinolone and more likely to exacerbate [10].

However, self-identified ethnicity did not affect asthma control test (ACT) scores or FEV₁ responsiveness to inhaled corticosteroids (ICS) in another study [11]. In another patient cohort with 5%

African ancestry, no genetic variants were associated with improvement of FEV₁ to ICS therapy [12[•]].

The discordant results above are unsurprising given that different aspects of corticosteroid responsiveness were examined in different studies. Ethnic differences in the responsiveness of airway inflammation to corticosteroids warrant further exploration.

Response to beta-agonists

Black patients are more likely than white patients to experience adverse asthma outcomes to long-acting beta agonists (LABA) therapy. In one study, only black patients who received salmeterol had a greater risk of respiratory-related death or life-threatening asthma compared with those who received placebo [13]. Among patients participating in various Asthma Clinical Research Network trials with LABA-containing treatment regimens, black patients had 2.36 the odds of white patients for experiencing treatment failure. No such increased odds were observed with non-LABA regimens [14].

The effect of polymorphisms on beta agonist responsiveness has been studied, especially that of the glycine-to-arginine (Gly-to-Arg) amino acid substitution at position 16 of the B2-adrenergic receptor gene (*ADBR2*). This polymorphism provides a potential explanation for ethnic differences in LABA responsiveness, as homozygosity of Arginine is more common in black patients. In a paediatric meta-analysis, each copy of the Arginine allele increased the odds for an asthma exacerbation by 1.52 in children treated with combined ICS/LABA, but not in those treated with ICS or leukotriene receptor antagonists (LTRA) alone [15]. However, a randomized trial of LABA vs. ICS/LABA combination in adults failed to demonstrate an effect of the Gly-to-Arg substitution on lung function outcomes. The study was not powered to detect differences in exacerbation or mortality rates between different genotypes [16].

The safety of LABA use has, therefore, not been fully confirmed in ethnic groups with a high prevalence of *ADRB2* gene polymorphisms.

Response to step-up therapy

For patients failing to achieve asthma control, guidelines currently recommend step-up treatment in a standardized fashion. However, emerging evidence suggests that ethnicity may influence response to step-up therapy. In a trial of children stepping-up from low-dose ICS to either high-dose ICS, or the addition of LABA or LTRA, Hispanic and non-Hispanic white patients responded most favourably to LABA but least favourably to high-dose ICS. Black patients were equally likely to respond to LABA or high-dose ICS, but least likely