The complexity of addressing racial and ethnic disparities

Racial and ethnic disparities in outcomes of in vitro fertilization (IVF) have been clearly delineated, with nonwhite women persistently experiencing a lower live birth rate (LBR) than their white counterparts (1). It is accepted that these disparities are likely the consequence of multiple compounding layers of inequalities, including differences in extrinsic factors such as access to care and insurance coverage, in addition to more intrinsic variations in biologic factors such as infertility diagnoses and associated comorbidities (2). The insightful investigation by Lee et al. (3) has highlighted the need to identify which components of the IVF process differ among races and ethnicities to better clarify contributing factors to the acknowledged disparities. They chose to evaluate specifically the interaction of race and ethnicity and response to gonadotropin stimulation using a standardized measure of ovarian responsiveness called the ovarian sensitivity index (OSI), which is calculated as the number of oocytes retrieved and total gonadotropin dose × 1,000. The OSI has been suggested to be a superior predictor of live birth compared with oocyte yield alone (4, 5). Variations in OSI on the basis of race and ethnicity were previously unknown, and therefore Lee et al. (3) sought to evaluate whether an association between race and ethnicity and OSI exists as well as the ability of differences in OSI to predict LBR.

Their hypothesis was that nonwhite race and ethnicity would be associated with lower OSI and lower LBR. Interestingly, in their analysis of 4,785 cycles, they found that adjusted OSI was higher in black and Hispanic patients compared with white patients. Although a lower LBR was noted for black patients compared with white patients in an unadjusted analysis, statistical significance did not persist in adjusted analyses. Similarly, the miscarriage rate was higher in nonwhite patients in the unadjusted analysis but again was not significant in the adjusted analyses. They also found that OSI modestly predicted live births overall. The OSI did not remain predictive for black or Hispanic patients as it did for white and Asian patients.

This study is important because it begins to look deeper into a specific factor that may ultimately be responsible for the disparate outcomes seen in black and Hispanic patients compared with white patients. Using the OSI as a discrete factor that adjusts ovarian responsiveness to gonadotropin dose controls for variabilities in dose and provides a standardized metric to evaluate oocyte yield and control for any differences that might exist. The OSI is but one of many clinical factors, however, that may be appropriate to investigate when looking for clinical parameters that might account for differences between races and ethnicities.

The limitations of the study were acknowledged by the investigators and focused primarily on many of the social determinants of health that are more difficult to identify in retrospective datasets. The dataset they used only presented data from a single institution, which was located within a state without mandated IVF insurance coverage, inherently inhibiting diversity in socioeconomic status within the population studied. Furthermore, these socioeconomic variables were not available in the dataset and therefore were not able to be characterized or controlled for in the adjusted analyses. A total of 70% of the patients were white, which undoubtedly contributed to many of the secondary outcomes not reaching statistical significance given the relatively few values within the minority race and ethnicity groups. Therefore, although their conclusions are noteworthy, they need to be interpreted in the context of this large but potentially less generalizable sample. This study also highlights the need to improve our ability to identify not only those clinical variables that might impact treatment outcomes but also the social determinants that may have significant effects as well.

By the nature of the primary outcome, which requires oocyte yield in its numerator, canceled cycles were excluded from the analysis. However, the cancelation rate was significantly higher among black patients, and black patients were more likely to cancel for reasons other than low or high response, such as financial difficulties, personal or family illness, or a change in decision to pursue IVF. This difference in cancelation rate may represent an additional reflection of underlying systemic disparities, and the exclusion of these patients in the analysis represents an inevitable selection bias. When the underlying socioeconomic factors that contributed to disproportionate cycle cancelation are similar to those that contributed to the observed variability in OSI and LBR, the observed effect may in fact underestimate the true disparity. Using OSI as a measure of ovarian responsiveness has a significant benefit in that it allows for a more contextual and standardized interpretation of the oocyte yield by accounting for the degree of ovarian stimulation, but the inherent limitation of needing to exclude canceled cycles in the analysis of this outcome restricts its use.

The conclusion drawn by Lee et al. (3) is that although black and Hispanic patients had greater ovarian responsiveness, they did not experience a consequent increase in LBR compared with white patients. Although it is interesting that a difference in ovarian responsiveness exists between racial and ethnic groups and that the underlying pathophysiology of these differences warrants further investigation, the more significant takeaway of this analysis is that the racial and ethnic disparity in IVF outcomes is unlikely to be attributable to differences in ovarian responsiveness. Progressively eliminating variables such as ovarian responsiveness as significant contributors to IVF outcome disparities allows for more efficient and effective direction of resources in both future research and efforts to address modifiable factors to minimize disparities. In this way, although this study did not identify a variable amenable to intervention, it has significantly contributed to the search for such a target. The acknowledgment by the investigators that certain socioeconomic factors may impact their data highlights the fact that disparities among racial groups are multifactorial. Lee et al. (3) highlighted the role of other clinical factors, such as uterine fibroids and endometrial implantation, as potential contributors to the observed disparities that deserve further study. In addition, it is important that we identify and include social determinants of health as variables we track so that we may ultimately study and

address whether they contribute to disparate outcomes and propose solutions to eliminate these inequities.

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