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EDITORIAL COMMENTARY

Commentary on "Trends and Racial Disparities for Acute Kidney Injury in Premature Infants: the US National Database"

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In "Trends and racial disparities for acute kidney injury in premature infants: the US national database," Dr. Elgendy and colleagues report that White preterm infants have significantly less acute kidney injury (AKI) than Black, Hispanic, or Native American infants [1]. While this is a novel finding, unfortunately, the increased prevalence of AKI among Black infants is in line with several recent publications describing disparities in NICU care and outcomes [2].

Well-described racial health disparities in maternal and neonatal health have been documented in the literature for decades. This phenomenon is disproportionately seen among Black births, where rates of prematurity are 1.5 times higher than non-Black births [2]. As the authors note, of central concern to the nephrologist when considering the kidney health implications of preterm birth is the arrest of nephrogenesis. In addition, other kidney health risk factors are of concern in the context of prematurity, including exposure to nephrotoxic medications, hemodynamic instability, delivery of proper nutrition, and infection. Low birth weight has also been identified as a risk factor for kidney disease in these children [3]. The increased rate of prematurity among Black babies when compared to non-Black babies could help to explain the AKI disparity described by the authors.

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The authors describe a novel disparity in AKI rates among premature neonates by racial category. Key to understanding this phenomenon is an appreciation of the close interplay between social determinants, pathologic risks inherent to prematurity, and resulting health outcomes. This relationship is important because it portends an upstream determinant of downstream disparity. What is more, an unhealthy through-line can be drawn across the spectrum of pediatric kidney disease: from the neonatal AKI disparities experienced by babies born prematurely, to kidney health disparities experienced by children with chronic kidney disease (CKD), and those who progress to stage 5 CKD. While there are several important points raised by this manuscript, we also would like to identify some opportunities for future research and advocacy.

Importance of terminology and language

Race is a social construct created and maintained by society. To a large extent by design, the term "race" represents a collection of people organized around a social identity as well as shared ancestry and phenotypic characteristics. Biological characteristics found to be different between races are thought to be due to differing frequencies of gene variants linked to ancestral geographic regions [4]. Patterns of expression of these gene variants are altered by physical, psychological, social, and environmental factors which have been historically and reductively grouped by skin color. As a social construct, there exists no biological basis for racial categorization, and as such, race-based pathologic conclusions are inherently fraught [5]. Thus, when studying outcomes by race, psychosocial and socioeconomic factors ideally should be explored when attempting to define associations with an outcome.

Black or African American people represent over 13% of the population in the USA. We note that there is nuance in racial vocabulary, and that the terms African-American and Black are often used interchangeably both in lay writing and research. The term African-American refers to those with

ancestral geographic lineage from the African diaspora and is rooted in the cultural underpinnings of American slavery. The term Black is a more inclusive term [4]. For this commentary, we will use Black, for consistency with the original article and for these reasons.

While racially disparate health outcomes are well-demonstrated across all care continua, it is widely accepted that these differences are not related to *race*, but instead to *racism* and its pervasive effects on life [6, 7]. This includes neonatal care and outcomes [2]. Racism is defined as a system of structuring opportunity and assigning value based on the social interpretation of how one looks (which is what we call 'race') that unfairly disadvantages some individuals and communities and unfairly advantages other individuals and communities [8]. As a social determinant of health, racism negatively contributes to neonatal outcomes by exacerbating the impact of structural adversity and institutionalized deprivation [9]. When it comes to adverse health outcomes in newborns, racism always makes health outcomes worse.

Disparities in the neonatal ICU and neonatal outcomes

Before talking about racial disparities in NICU outcomes, racial disparities in pregnancy and preterm birth rates need to be addressed. Black women are three times more likely than White women to die from pregnancy-related causes, Black babies are more than twice as likely as White babies to die before 1 year of age, and non-White women are up to 1.5 times more likely to give birth prematurely [10]. Despite increased attention to these issues, disparities in preterm birth rates have worsened over the past decade [10]. This is a complex issue with contributions from maternal health, management of pre-existing conditions, and social determinants of health, such as health care coverage, poverty, and access to prenatal care. In this article, Elgendy and colleagues hypothesize that the increased rates of AKI in premature Black infants may be secondary to utilization of prenatal care. While this is one possibility, this disparity may also be related to lack of access to prenatal care or equitable care compared to non-Black mothers. Further research and careful analysis are needed to determine how other racial factors affecting pre-pregnancy care, pregnancy care, and preterm birth rates may be playing a role in the disproportionate AKI prevalence in the NICU.

Furthermore, Black, Hispanic, and Asian infants are segregated among NICUs and are treated in units with lower quality scores [11]. While racial and ethnic disparities have improved in extremely preterm infants over the last two decades, significant gaps remain [12]. For example, Black women have twice the risk of having a low birth weight infant than non-Black women [13]. Similarly, the risk of preterm birth and higher mortality still exist among Black women when evaluating trends over the past five decades [14]. In order to identify and begin to address these disparities in the NICU, Horbar and colleagues have delineated specific actions that can be taken and are organized into six discrete categories [15]. In Table 1, we have used these categories and applied them specifically to the diagnosis of AKI in the NICU.

Importance of AKI Identification in the NICU

In their article, Dr. Elgendy and colleagues report a prevalence of AKI of 1.5% in prematurely born infants. We note that this prevalence is from the National Inpatient Sample (NIS) and is solely based on ICD-9 and ICD-10 coding. This rate of recognized AKI is dramatically lower than studies of similar patient populations which determined AKI based on serum creatinine change or urine output decreases [16]. Previous studies, such as Assessment of Worldwide Acute Kidney Injury Epidemiology in Neonates (AWAKEN), found rates of close to 40% among high-risk infants born < 28 weeks [16]. The low AKI prevalence in this article is similar to other studies which have shown that AKI is underappreciated by neonatologists, and studies which rely on documentation in the medical record likely under-report AKI [17, 18].

This article is the first to report racial disparities in AKI among infants, finding that Black infants had a higher prevalence of AKI diagnosis than White infants. Multiple studies have demonstrated that Black infants are more likely to be small for gestational age or have intrauterine growth restriction than their White peers [12]. Due to this, it is challenging to unequivocally state which is the underlying, or causal, risk factor. We note that the AWAKEN study did not report a statistically significant difference in AKI prevalence between Black and White infants [19]. However, the findings of this article are similar to database-based reporting of AKI in pediatric patients, where Black pediatric patients had a greater representation of AKI hospitalizations [20]. Further research and analysis, especially that utilize causal inference methodology to determine the independent effect of factors that are components of larger complex systems, are urgently needed to address these issues [21].

It is also important to note that disparities in AKI are not the same as disparities in AKI reporting. Low rates of AKI reporting in infants are multifactorial in nature, as there are multiple steps between an infant having AKI and a neonatologist making a diagnosis of AKI in the medical record. First, an infant has to be recognized as high risk for AKI. Large studies have used various criteria to stratify risk of

Table 1 Suggestions for Improved NICU practices for Infants with AKI

General NICU	AKI specific
Promote a culture of equity	- Provide AKI education that reaches all NICU parents regardless of race - Develop AKI education for providers that is independent of race-related risk factors - Acknowledge implicit personal bias when caring for infants in the NICU - Create an AKI NICU disparities dashboard
Identify social risks of families and provide interventions to prevent and mitigate those risks	- Create alliances with community organizations to teach about AKI, preterm risks
Take action to assist families after discharge (transition home)	- Tailor education on long-term AKI outcomes to each family's needs - Improve communication with families about AKI and CKD risk - Provide ongoing nephrology follow-up for infants with AKI to improve early identification of CKD - Partner with primary care providers to provide care for infants with AKI to decrease barriers to follow-up care
Maintain support for families through infancy	- Ensure nutritional and medication programs are available for those with a history of AKI - Improve communication of AKI diagnosis to providers in order to optimize appropriate CKD surveillance
Develop robust QI efforts to ensure equitable, high-quality hospital and follow-through care to all newborns by eliminating modifiable disparities	- Establish measurable improvement aims related to social determinants of neonatal AKI
Advocate for social justice at the local, state and national levels	- Disseminate research on disparities in AKI diagnosis - Educate organizational leaders on social determinates of AKI - Name racism: how is racism affecting neonatal AKI diagnosis?

AKI acute kidney injury, *CKD* chronic kidney disease, *NICU* neonatal intensive care unit, *QI* quality improvement

AKI. For example, the AWAKEN study considered infants receiving intravenous fluids for at least 48 h to be high risk [22]. Others have advocated expanding these criteria to those needing invasive respiratory support, more than 48 h of intravenous antibiotics, or at times of events (such as necrotizing enterocolitis or patent ductus arteriosus treatment with indomethacin) which may increase the risk of AKI. Secondly, serum creatinine and urine output must be closely monitored in order to detect changes in kidney function. There is significant variation in frequency and intensity of serum creatinine and urine output monitoring between NICUs based on differences in clinical practice [23]. There is not yet a standardized approach to serum creatinine or urine output assessments, which further complicate the diagnosis of AKI. Finally, even if AKI is detected by serum creatinine or urine output change, these changes must be noted by the care team and recorded in the medical record in order to be provider recognized. Studies have found that only 10–30% of infants with AKI are diagnosed by their care team [17, 18]. We note with significant concern that there are multiple opportunities throughout these steps that are inherently at risk of implicit bias, for example the frequency of serum creatinine measurement. Each of these is an opportunity to improve equitable provision of care (Table 1).

Disparities in AKI to CKD

The disparities in neonatal AKI reported by Elgendy and colleagues are important because they not only have significant early life implications but also consequences along the life course. Pediatric AKI has also been shown to occur more frequently in Black children and adults, though this is one of the first studies to demonstrate this disparity in neonates with AKI [24, 25]. Genetic risk variants of the apolipoprotein L1 (*APOL1*) gene are often cited as an explanation for the disproportionate frequency of AKI among Black persons; however, this association is not consistent in AKI literature. In a large adult study demonstrating a disproportionate incidence of AKI among Black persons, accounting for income and insurance status attenuated the risk of AKI among Black persons [24]. There was no association between the presence of high-risk *APOL1* gene variants and AKI among Black adults. Given that the majority of individuals who carry the high-risk *APOL1* genotype do not have kidney disease, greater exploration of socioeconomic factors and racial biases in pediatric AKI is warranted. For the neonatal population, this may also suggest a larger influence of maternal in utero factors rather than genetics.

AKI has also been shown to lead to irreversible kidney injury and decreased kidney function. This is thought to predispose to additional episodes of both AKI and CKD that may manifest in late childhood or adulthood. Research has shown that up to 50–60% of children with AKI experience the long-term sequelae of CKD [26, 27]. The pathophysiology underlying AKI to CKD progression is multifactorial and thought to be dependent upon patient background including severity, duration, and prior frequency of AKI events [28]. These changes may be more notable in prematurely born infants due to decreased nephron number (oligonephronia) and reduction in future development of nephrons due to premature birth [29]. These factors make early life exposure to AKI especially problematic for life course and the development of CKD. The identification of AKI among infants is essential in order to allow for appropriate monitoring for CKD. In addition, there is a propensity for more rapid progression to stage 5 CKD in Black children and adults. Unlike studies of AKI in Black Americans, many adult and pediatric studies have shown an association between *APOL1* gene variants and CKD. Nevertheless, only 13% of the US Black population carries the *APOL1* high-risk genotype, highlighting the importance of additional research beyond race and the *APOL1* genetic variant in kidney disease.

Given the increased risk of CKD in those born prematurely, appropriate identification and communication of a diagnosis of AKI is essential to improve ongoing outpatient management and care for infants. Theoretical models show how interactions between social determinants of health (i.e., psychosocial and environmental factors), racial biases, and the presence of the *APOL1* genotype in individuals of African descent may contribute to the heightened CKD risk [30]. Knowing these factors and understanding how they contribute to the risk of AKI is critical to instituting healthcare policies and guidelines to reduce AKI and ultimately CKD disparities. Future research is needed to assess social determinants of health and other factors beyond race and the association with AKI.

Disparities in pediatric stage 5 CKD

As children with neonatal AKI age, they are at increased risk of progressive CKD including stage 5 CKD, where they face additional racial health disparities that impact outcomes. In addition to facing troubling neonatal disparities, Black children experience a time to dialysis initiation that is 38% shorter, but a time to transplant that is 54% longer than their non-Black counterparts [3]. Post-transplant, these disparities persist: Black children are 50% more likely to have kidney allograft failure and are more likely to experience acute allograft rejection [3]. In fact, allograft failure rates for Black children are higher than non-Black children after controlling for co-variates like socioeconomic and private versus public insurance status [31]. Disrupting this chain may require nephrologists to intervene beyond biological determinants of health and begin to address the social determinants of health as well.

The quest to eliminate racial disparities in neonatal AKI outcomes is unlikely to result in the identification of some elusive allelic variation that predisposes Black babies to this adversity. Instead, it will likely require an "all hands-on deck" approach to decreasing the incidence of preterm birth, and mitigating the harm of structural racism and other social determinants of health on neonates both inside and outside of the NICU [32].

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