GFR, Organ Donation and Transplantation: BAME Inequalities

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BRIEF BIOGRAPHY

- Born in Winchester, UK to Bangladeshi parents – 1st generation
- Grew up in the North West, in Newton-le-Willows (between Manchester & Liverpool)
- Only non-Caucasian and non-Christian in a school of 1000 pupils (save younger brother)
- Initially only family member with University education
- Now growing number of educational advancement in the Bangladeshi community

BRIEF BIOGRAPHY

- Undergraduate training at University of Sheffield
- Postgraduate surgical training in Liverpool, Manchester, Sheffield & Leeds
- MSc (Stem Cells & Regeneration) University of Bristol
- PhD (Molecular Oncology & Radiobiology) University of Oxford
- NIHR Lecturer in Surgery at University of Manchester
- Appointed Consultant Transplant & Access Surgeon at St. George's, London in March 2020
- Appointed Honorary Senior Lecturer to St. George's Medical School, University of London in July 2020
- Co-lead for the Introduction to Medicine Module

ORGAN DONATION

- New figures from NHSBT reveal that 121 people from these ethnic backgrounds donated their organs after they died last year, the highest number to date
- This figure has increased by 51% in the last five years
- And 969 BAME patients received an organ from a deceased donor last year, accounting for a quarter of all deceased donor transplants

ORGAN DONATION

- But there is still a stark imbalance between the numbers of BAME donors and those patients in need of a lifesaving transplant
- People from these communities represented 8% of all deceased donors last year compared with 31% of those on the transplant waiting list
- Average UK waiting time for a kidney is 2.5 years and for BAME patients this is 3 years
- Average St. George's time is 3 years and for BAME patients this is 3.5 years

GFR

- Is the test itself inherently racist i.e. created with the intent to deliberately disadvantage black patients?
- Is it a case of flawed data and scientific foundations?
- Can the test be used in a racist way?
- Does the test actually disadvantage black patients or potentially give them the advantage?

GFR

JAMA. 2019 Jun 6. Doi: 10.1001/jama.2019.5774. [Epub ahead of print]

Reconsidering the Consequences of Using Race to Estimate Kidney Function.

Eneanya ND, Yang W, Reese PP

EGFR

- This test has traditionally used the Modification of Diet in Renal Disease (MDRD) or Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations to calculate eGFR to determine levels of creatinine in each sample
- Both use race, gender, age and serum creatinine – MDRD was calculated with self-reporting of race whilst the CKD-EPI used cohort studies (small sample!)
- Other methods used the Cockcroft-Gault formula which used weight instead of race
- Found to be inaccurate in the ‘black’ population
- Also those with amputations, ascites etc.

GFR

STAGES OF CHRONIC KIDNEY DISEASE		GFR*	% OF KIDNEY FUNCTION
Stage 1	Kidney damage with **normal** kidney function	90 or higher	
Stage 2	Kidney damage with **mild loss** of kidney function	89 to 60	
Stage 3a	**Mild to moderate** loss of kidney function	59 to 45	
Stage 3b	**Moderate to severe** loss of kidney function	44 to 30	
Stage 4	**Severe** loss of kidney function	29 to 15	
Stage 5	Kidney **failure**	Less than 15	

* Your GFR number tells you how much kidney function you have. As kidney disease gets worse, the GFR number goes down.

GFR

Measuring kidney function

Creatinine-based estimate of GFR

1.1.1 Whenever a request for serum creatinine measurement is made, clinical laboratories should report an estimate of glomerular filtration rate (eGFRcreatinine) using a prediction equation (see recommendation 1.1.2) in addition to reporting the serum creatinine result[2]. **[2014]**

1.1.2 Clinical laboratories should:

- use the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation to estimate GFRcreatinine, using creatinine assays with calibration traceable to standardised reference material
- use creatinine assays that are specific (for example, enzymatic assays) and zero-biased compared with isotope dilution mass spectrometry (IDMS)
- participate in a UK national external quality assessment scheme for creatinine. **[new 2014]**

For more information about implementing this recommendation, see implementation: getting started.

1.1.3 Apply a correction factor to GFR values estimated using the CKD-EPI creatinine equation for people of African-Caribbean or African family origin (multiply eGFR by 1.159). **[new 2014]**

1.1.4 In people with extremes of muscle mass – for example, in bodybuilders, people who have had an amputation or people with muscle wasting disorders – interpret eGFRcreatinine with caution. (Reduced muscle mass will lead to overestimation and increased muscle mass to underestimation of the GFR.) **[2008]**

GFR

- It is frequently assumed that the higher serum creatinine observed in black persons is secondary to ‘greater muscle mass’. What is less certain is whether more skeletal muscle in black persons truly accounts for higher serum creatinine across the spectrum of chronic kidney disease. In a 2008 study, Hsu et al took almost 3000 hemodialysis patients (~50% of the population were black) and sought to determine if the higher serum creatinine observed in black patients was secondary to body composition (assessed by bioelectrical impedance).
- Interestingly, they found no such association (after controlling for age, nutritional status and dialysis vintage).
- Regardless of the mechanism underlying higher serum creatinine, both the MDRD and CKD-EPI studies demonstrated a higher *measured* GFR in black persons for a given serum creatinine. This is hard to ignore.

BLACK PEOPLE & MUSCLE MASS

ACTN3 has two key variants: R and X. To recap:

> Roughly speaking, the more copies of the R variant you have, as opposed to the X variant, the more likely you are to excel at sports requiring power or speed. (You can be RR, RX, or XX.) The testing company, Atlas Sports Genetics, cites studies that support this pattern. A 2003 analysis of hundreds of athletes who had represented Australia at international meets found that 53 percent of the male competitors in sprinting or power events were RR—nearly twice the prevalence of this genotype in a less-athletic population sample. None of the 35 female sprinters were XX. Nor were any of the 25 male Olympic sprinters. Subsequent studies show the same basic pattern in Finland, Greece, and Russia.

Few genes are known to be decisive in determining life outcomes. Nutrition, training, and other genes matter. But the evidence that this gene significantly influences athletic ability is strong.

Now look at the frequency of the R and X variants in different populations. According to data published seven years ago in *Human Molecular Genetics*, the relative frequency of the X allele is 0.52 in Asians, 0.42 in whites, 0.27 in African-Americans, and 0.16 in Africans. If you break out the data further, the frequency of the XX genotype is 0.25 in Asians, 0.20 in European whites, 0.13 in African-Americans, and 0.01 in African Bantu. Conversely, the frequency of RR (the genotype for speed and power) is 0.25 in Asians, 0.36 in European whites, 0.60 in African-Americans, and 0.81 in African Bantu. Among Asians, you can expect to find one RR for every

GFR

- CKD-EPI equation has been adapted for different populations
- This study of 130 Indians (roughly half of whom were vegetarians) found that the CKD-EPI did overestimate GFR in that population.
- Japanese study suggests their population has a GFR which is about 80% of that estimated from the CKD-EPI equation
- Another study from Pakistan suggests the correction factor should be 0.686. Thus, studies from India, Japan and Pakistan suggest that the measured GFR is lower than estimated using the CKD-EPI equation for whites. This is in contrast to the CKD-EPI validation suggesting 5% higher measured GFR in Asians.

GFR

	White	Black
Serum creatinine µmol/l (mg/dL)	250 (2.8)	250 (2.8)
Age	55	55
Sex	F	F
Weight (kg)	80	80
Height (cm)	160	160
BSA (m^2)	1.89	1.89
Cockroft-Gault (ml/min)	28	28
MDRD (ml/min/1.73m^2)	18	22
CKD-EPI (ml/min/1.73m^2)	18	21
CKD-EPI (de-indexed) (ml/min)	20	23

GFR: IMPLICATIONS

- When to refer to nephrology
- Dosing of antibiotics and other medications
- When is it safe to use iodinated and gadolinium-based contrast agents
- When can patients be listed for a kidney transplant
- The timing of dialysis planning and initiation
- Inclusion in clinical trials

FURTHER INFORMATION

Organ donation among ethnic minorities: how UK primary care can help promote it

Agimol Pradeep, Abul Siddiky, Paula Ormandy and Titus Augustine

British Journal of General Practice 2018; 68 (668): 134-135. **DOI:** https://doi.org/10.3399/bjgp18X695093

A career in transplant surgery

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