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The prevalence of hematologic and metabolic abnormalities during chronic kidney disease stages in different ethnic groups

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We conducted an observational cross-sectional study to determine if the prevalence of hematologic and metabolic abnormalities in chronic kidney disease (CKD) varied in different ethnic groups. We used a CKD provincial database where a complete data set at the time of registration was available as well as an estimated glomerular filtration rate (eGFR), which showed using the abbreviated MDRD formula that the patients had CKD of stages 3–5. We included patients with self-reported race of Caucasian, Oriental Asian, or South Asian. Primary outcomes were the prevalence of at least one of the following: anemia, hypocalcemia, hyperphosphatemia, hyperparathyroidism, hypoalbuminemia, and three or more laboratory abnormalities. All definitions were consistent with K/DOQI guidelines. When compared with Caucasians, Oriental Asians and South Asians had a higher prevalence of many of the metabolic abnormalities during most stages of CKD and were more likely to have any abnormality at all levels of eGFR. The prevalence of three or more laboratory abnormalities was higher in Oriental Asians at all stages and in South Asians at some levels of eGFR. These results were unchanged or exaggerated when controlled for age, gender, diabetes, and a primary diagnosis of renal disease. Hence, it appears that South Asians and Oriental Asians have more laboratory abnormalities compared with Caucasians at most levels of eGFR.

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Chronic kidney disease (CKD) is associated with increased morbidity and mortality.[1] The majority of deaths, both in patients on renal replacement therapy and in pre-dialysis patients, are due to cardiovascular events.[2] The presence of CKD has been shown to be a strong predictor of future cardiovascular events, independent of traditional risk factors.[2–4] It is not clear what accounts for this increased risk. There are many metabolic abnormalities that develop with progressive renal parenchymal damage, including calcium, phosphate, parathyroid hormone, albumin, and hemoglobin disturbances. It is not known which, if any, of these abnormalities accounts for the increased cardiovascular disease risk, or whether treating these abnormalities can alter morbidity and mortality rates.

The metabolic abnormalities related to CKD (including anemia, hypocalcemia, hyperphosphatemia, and hyperparathyroidism) are associated with increased risk to the patient.[4–10] These risks are for the development of other conditions (cardiovascular disease, susceptibility to infection, bone disease), as well as progression of kidney disease to end stage. However, at any given level of eGFR, there is much heterogeneity in the severity of metabolic abnormalities. For example, in CKD stage 5, 25% of patients have a hemoglobin level above $110\,g\,l^{-1}$ (the recommended lower limit of the target hemoglobin level).[6,11] In end-stage renal disease patients, 15% have normal bone biopsies with no evidence of osteitis fibrosa cystica, aplastic bone disease, or osteomalacia.[12] These observations suggest a disconnect between the filtration function of the kidney (as measured by GFR) and the hormonal function of the kidney (as measured by various metabolic abnormalities).

One possible explanation for such heterogeneity might be ethnicity, which has been shown to affect various outcomes in renal disease. Among peritoneal dialysis patients, Blacks have significantly lower hemoglobin levels compared to nonblacks despite receiving more treatment for anemia.[13] At each of CKD stages 3–5, anemic patients (defined as hemoglobin $<110\,g\,l^{-1}$) are more likely to be Caucasian than they are Asian, with the majority of anemic patients

being Caucasian.[6] Furthermore, the long-term outcome of patients on dialysis has been shown to be impacted by ethnicity, with Asians having the best outcomes when compared with age- and gender-matched controls on dialysis.[14,15]

As metabolic abnormalities are associated with poor outcomes, and ethnicity is known to predict survival, we hypothesize that the number of metabolic abnormalities at each stage of CKD may vary by ethnicity. We sought to investigate this further by describing the metabolic abnormalities in Asians and Caucasians at each stage of CKD, a relationship that has yet to be reported in the literature.

RESULTS

Derivation of the cohort and characteristics

The entire database contains 15 346 registered patients. The primary criteria for establishment of the cohort were the availability of self-reported race (SRR), complete laboratory data, and eGFR <60 ml per min per 1.73 m^2 within the prespecified date range, which were available for 5536 patients. Figure 1 describes the final derivation of the analytical cohort, which excluded patients with SRR other than Asian Orientals, South Asians, and Caucasians (e.g. Filipino and First Nations); thus a total of 5322 patients were available for analysis. Of note, analyses that included patients without an available SRR were not significantly different than those that excluded them; thus concerns about biased sample are relatively minor. This is addressed further in the discussion. The final cohort thus included 4047 Caucasians, 763 Oriental Asians, and 512 South Asians. The baseline characteristics of the different SRR groups are shown in Table 1. There are statistical differences between SRR for baseline eGFR, age, sex, diabetes, and primary diagnosis of kidney disease. The absolute differences in eGFR were small, so we examined the ethnic mix at each level of eGFR. Figure 2 shows that the relative proportion of each SRR across levels of eGFR is similar.

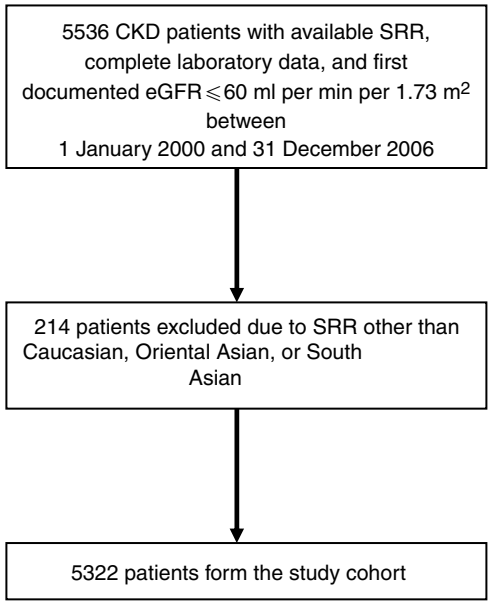

Figure 1 | Analytical cohort derivation from the Provincial Registry of all CKD patients. SRR, self-reported race.

Laboratory abnormalities

The data describing the median values for calcium, phosphate, parathyroid hormone, hemoglobin, and albumin are shown in Table 2; Figure 3 displays similar data graphically, using the prevalence of abnormalities as defined by K/DQOI cut-offs, in percentages. The interaction terms for SRR and eGFR were significant for PO_4 and Alb (both P-values <0.03) but not for Hb, Ca, and intact parathyroid hormone (iPTH); that is, the effect that race has on Hb, Ca, and iPTH holds true at all levels of eGFR. The percentage of patients who are anemic was significantly different across SRR ($P<0.01$); Oriental Asians were 1.4 times more likely to be anemic than Caucasians (95% confidence interval (CI) for odds ratio (OR): 1.2–1.7), with no difference between South Asians and Caucasians (OR: 1.0, 95% CI for OR: 0.8–1.3). The results for hypocalcemia follow the same pattern as those for anemia; the odds for hypocalcemia in Oriental Asians were almost two times the odds in Caucasians (95% CI for OR: 1.4–2.6). Hyperparathyroidism was also statistically different between SRR ($P<0.01$), with both South Asians (OR: 1.5, 95% CI for OR: 1.3–1.8) and Oriental Asians (OR: 2.2, 95% CI for OR: 1.8–2.7) more likely to be hyperparathyroid than Caucasians.

The interaction terms for SRR and eGFR were significant for hyperphosphatemia and hypoalbuminemia, suggesting that the effect of SRR on these metabolic abnormalities may vary at some levels of eGFR. The percentage of patients with hyperphosphatemia was found to be different by SRR only at eGFR levels of 15–30 and 30–45 ml per min per 1.73 m^2 (both P-values for SRR <0.01). For an eGFR of 15–30 ml per min per 1.73 m^2, South Asians were more likely to be hyperphosphatemia than Caucasians (OR: 1.8, 95% CI for OR: 1.2–2.7), with no difference between Oriental Asians and Caucasians. For an eGFR of 30–45 ml per min per 1.73 m^2, Oriental Asians had higher odds of being hyperphosphatemia than Caucasians (OR: 2.5, 95% CI for OR: 1.4–4.5), with no difference between South Asians and Caucasians. The percentage of patients with hypoalbuminemia was significantly different by SRR only at eGFR levels of <15 and 15–30 ml per min per 1.73 m^2 (both P-values for SRR <0.01). For an eGFR of 15–30 ml per min per 1.73 m^2, both Oriental Asians and South Asians were 1.5 times more likely hypoalbuminemia than Caucasians (95% CI for OR: 1.2–2.0), whereas for an eGFR of <15 ml per min per 1.73 m^2, the odds were much lower in South Asians (OR: 0.4, 95% CI for OR: 0.3–0.7).

The association between the presence of 'any laboratory abnormality' and SRR did not vary by eGFR levels (P-value for the SRR/eGFR interaction $=0.24$). The proportions were found to be different by SRR ($P<0.01$); specifically, both Oriental Asians and South Asians were more likely to have