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Racial-ethnic differences in chronic kidney disease-mineral bone disorder in youth on dialysis

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Abstract

Background: Studies in healthy pediatric populations and adults treated with dialysis demonstrate higher parathyroid hormone (PTH) and lower 25-hydroxyvitamin D levels in African-Americans. Despite these findings, African-Americans on dialysis demonstrate greater bone strength and a decreased risk of fracture compared to the Caucasian dialysis population. The presence of such differences in children and young adult dialysis patients is unknown.

Methods: Differences in the markers of mineral and bone metabolism (MBM) were assessed in 661 incident dialysis patients (aged 1 month to <21 years). Racial-ethnic differences in PTH, calcium, phosphate and total alkaline phosphatase (AP) activity were analyzed over the first year of dialysis using multivariate linear mixed models.

Results: African-American race predicted 23% higher serum PTH (95% CI, 4.7 – 41.3%) when compared to Caucasian patients, while Hispanic ethnicity predicted 17.5% higher PTH (95% CI, 2.3 – 38%). Upon gender stratification, the differences in PTH were magnified in African-American and Hispanic females: 38% (95% CI, 14.8 – 69.8%) and 28.8% (95% CI, 4.7 – 54.9%)

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higher PTH compared to Caucasian females. Despite higher PTH values, African-American females persistently demonstrated up to 10.9% lower serum AP activity (95% CI, −20.6 - −0.7%).

Conclusions: There are racial-ethnic differences in the markers of MBM. Higher PTH is seen in African-American and Hispanic children and young adults on dialysis with a magnification of this difference amongst the female population. There is a need to consider how factors like race, ethnicity and gender impact the goal-targeted treatment of MBM disorders.

Keywords

Biochemical markers of bone turnover; Parathyroid-related disorders; Chronic Kidney Disease-Mineral Bone Disease; Children; Dialysis

Introduction

Management of the markers of mineral and bone metabolism (MBM) has important implications on the skeletal and cardiovascular health of children and young adults with chronic kidney disease (CKD). As in adults with CKD, the skeletal and cardiovascular systems interact to determine the prevention of, or propensity toward, vascular calcification and cardiovascular remodeling. The maladaptive interaction of these systems provides a major mechanism for the 1000-fold increased risk of cardiovascular death seen in pediatric patients on dialysis when compared to the general pediatric population [1]. Interestingly, major markers of MBM, particularly, serum parathyroid hormone levels (PTH), 25-hydroxyvitamin D (25-OHD) and Alkaline Phosphatase (AP) have been shown to differ by race and ethnicity in the healthy pediatric population. For instance, healthy African-American children have higher PTH, lower 25-OHD and higher AP levels than Caucasian children [2–4]. Despite the fact that this biochemical profile might suggest poorer bone health, African-American children demonstrate greater bone strength as evidenced by greater markers of bone formation, lower markers of resorption and greater bone mineral density (BMD) [3, 5–8].

Differences in MBM markers have also been demonstrated in the adult population, including in adults with pre-dialysis CKD and on maintenance dialysis [9, 10]. In the adult CKD population, African-Americans demonstrate higher PTH and AP than both Caucasian and Hispanic patients, yet African-Americans demonstrate a lower risk of fracture compared to Caucasian patients [11–18]. The paradox between biochemical measures and skeletal outcomes underscores the need to further explore these differences, particularly in the pediatric CKD population in whom little is known. Given the reliance on biochemical measures to provide treatment, it is essential to understand the contribution of race and ethnicity to MBM markers. Thus, in the first step toward exploring these racial-ethnic differences in MBM in pediatric patients with CKD, we seek to compare biochemical markers of MBM across race and ethnicity within a pediatric dialysis population.

Materials and methods

Study participants

The source cohort consisted of patients receiving care at any one of the dialysis facilities of a large national dialysis organization (LDO) between October 1, 2006 and December 31, 2011. Institutional Review Board approval was obtained from the University of California, Irvine. Given the lack of patient identifiable information and the lack of patient burden, consent was exempted in this study. Construction of our cohort is illustrated in Figure 1. After removing patients with missing race-ethnicity, age, and those ages 21 years or older, 1901 patients remained. In order to assess trends in PTH, the cohort was further narrowed to incident patients who at minimum had a PTH measurement at baseline and at 6 months post-dialysis initiation. Patients with a reported race-ethnicity other than Caucasian, African-American or Hispanic were excluded due to their small sample size. The final study population consisted of 661 incident children and young adult dialysis patients.

Demographic, clinical, and laboratory measures

All data were obtained from the electronic medical records of the LDO. The primary exposure, race-ethnicity, was determined by self-report from the patient or parent. Cause of end-stage renal disease (ESRD) was categorized as congenital anomalies of the kidney and urinary tract (CAKUT), glomerulonephritis (GN) and other/unknown, the majority of which were unknown. Clinical measures including weight in kilograms, and laboratory measures including the primary outcome, PTH, and secondary outcomes of albumin-corrected calcium, phosphate and AP were obtained from the electronic medical record of the LDO. All laboratory determinations were routinely drawn and processed according to standard procedures at a laboratory in Deland, FL. Laboratory measurements are reported as quarterly averages in order to minimize the impact of single measurement outliers. Patient quarters are defined by 13-week intervals and patients were analyzed over the first 4 quarters of dialysis corresponding to the first year of treatment on dialysis. Values during the first 13-week interval were considered as baseline.

Medication use, including nutritional vitamin D, calcium-based binders, non-calcium-based binders and cinacalcet, was assessed within the first quarter of dialysis. Use of active vitamin D sterols including paricalcitol, doxercalciferol and calcitriol was assessed across the first year of dialysis. Dosages of paricalcitol and doxercalciferol were converted to calcitriol-equivalent doses using a multiplication factor of 0.25 and 0.42, respectively, according to reference materials [19, 20]. For each quarter of dialysis, the sum of all calcitriol-equivalents was normalized to body weight in kilograms.

Statistical analyses

Baseline characteristics including laboratory measurements are reported as means ± standard deviations or medians and interquartile ranges for continuous, normally distributed and non-normally distributed variables, respectively. Differences between racial-ethnic groups in these variables were determined by Analysis of Variance (ANOVA) and Kruskal-Wallis tests, where appropriate. Categorical variables are reported as frequency and percentages and

differences analyzed using chi-square analysis or Fisher Exact test (for cell sizes less than 5). For all analyses, a corresponding p-value of less than 0.05 denotes significance.

Linear regression models were used to determine predictors of PTH, serum calcium, serum phosphate and AP within the first 13 weeks of dialysis. PTH and AP were $\log_{10}$-transformed when used as outcomes in order to achieve a symmetric distribution for each variable. For log-transformed outcomes, in all models, regression coefficients are expressed as percent differences according to the formula: $[(10^{B})-1]*100$. Phosphorus and AP z-scores were created using age-based norms for phosphate, and sex- and age-based norms for AP, from the healthy population [21]. Covariates included race-ethnicity, age, gender, modality of dialysis, cause of ESRD, serum PTH level, serum calcium level, serum phosphate z-score, serum AP z-score, and cinacalcet usage (for PTH and calcium models), the only medication at baseline which differed significantly between racial-ethnic groups.

A multivariate, linear mixed model was used to determine the association of race and ethnicity with MBM markers over the first year of dialysis and to account for the correlation of repeated measurements in the same subject. The covariates for linear mixed models were the same as for the linear regression models with the addition of interactions between race-ethnicity and time, when significant. The appropriate covariance matrix structure was determined by minimization of the Bayesian Information Criterion (BIC) for each model. Results of the linear mixed models were stratified by gender to assess for a differential impact of gender on the relationship between race-ethnicity and MBM markers.

Sensitivity analyses were performed to determine the potential impact of active vitamin D administration, serum 25-OHD levels and age on differences in PTH. To evaluate the potential impact of differential administration of active vitamin D sterols on the relationship between race-ethnicity and MBM markers, a sub-analysis of hemodialysis (HD) patients was undertaken because data on intravenous administration of active vitamin D was available. In this sub-cohort, linear mixed models were repeated with the above covariates and the addition of active vitamin D dosing normalized for body-weight.

Aside from the assignment of “unknown” to subjects with unreported causes of ESRD, missing values were assumed to be missing at random and were not interpolated. Therefore, due to missing covariates - modality, AP and/or calcium - 12 subjects were not included in each fully-adjusted regression model. All statistical analyses were conducted using SAS, version 9.4 (SAS Institute, Inc., Cary, NC, USA).

Results

Cohort characteristics

The cohort characteristics by racial-ethnic group are described in Table 1. A total of 661 patients were included of which 206 (31%) were African-American, 222 (34%) were Caucasian and 233 (35%) were Hispanic. The median (Interquartile Range or IQR) age was 19 (16–20) years and 54.6% of patients were male. 502 (76.3%) patients received hemodialysis (HD) as their initial modality and 156 (23.7%) were treated with peritoneal dialysis (PD). HD as the primary modality was most common amongst African-Americans

and PD was utilized more often in Hispanics. There was no difference in the frequency of use of calcium-based binders, non-calcium based binders and nutritional vitamin D between the groups at baseline. Cinacalcet use, though infrequent, was highest amongst Caucasian patients.

Baseline markers of mineral metabolism

In linear regression analysis of baseline values using Caucasian patients as the reference group, African-American race and Hispanic ethnicity were associated with a 23% (p=0.004) and 25.9% (p=0.003) higher PTH than Caucasian patients. Hispanic ethnicity significantly predicted lower serum calcium and was associated with a 0.22 mg/dL (p=0.0003) lower calcium level when compared to Caucasian subjects. Both African-American race and Hispanic ethnicity predicted lower serum phosphate levels than Caucasians: 0.46 mg/dL (p=0.0003) lower in African-Americans and 0.28 mg/dL (p=0.03) in Hispanics. African-American race was associated with an 8.8% (p=0.02) lower AP than Caucasian patients although there was no difference in AP between Hispanic and Caucasian children.

Differences in MBM markers over time

In a linear mixed model of repeated measures over the first year of dialysis, similar patterns of MBM markers emerged. PTH during the first year of dialysis was 23% higher in African-Americans when compared to Caucasians and 17.5% higher in Hispanics when compared to Caucasians (Table 2). Tests for an interaction between race-ethnicity and time showed that serum PTH levels were associated with differential change over time by race-ethnicity (Figure 2). PTH in African-Americans remained higher over time whereas the PTH in Hispanic and Caucasian patients progressed toward similar values (p for interaction = 0.003).

Compared to Caucasian patients, serum calcium levels were 0.2 mg/dL lower in Hispanic patients and did not differ in African-American patients (Table 2). Both African-American and Hispanic patients had lower serum phosphate concentrations over the course of the first year of dialysis: 0.46 mg/dL lower in African-Americans and 0.34 mg/dL lower in Hispanics. Results were similar when modeled using phosphate z-scores. African-Americans demonstrated an 8.8% lower AP when compared to Caucasian patients, whereas Hispanics did not show a significant difference. The interaction between race-ethnicity and time was not significant for serum calcium, phosphate or AP. Geometric means for the study period and the associated confidence intervals for PTH, calcium, phosphate and AP are presented in Figure 3.

Stratification by gender revealed modification of the relationship between race-ethnicity and MBM markers (Table 3). Notably, differences in PTH were most dramatic in African-American and Hispanic females who had 38% and 28.8% higher PTH when compared to Caucasian females, respectively. Calcium, phosphate levels and AP also differed by gender (Table 3).

Sensitivity analyses

Three sensitivity analyses were undertaken to determine the consistency of PTH findings. Firstly, to assess for the possible impact of the dosing of active vitamin D sterols on the primary outcome, PTH, in the first year of dialysis, 493 hemodialysis patients with available weight-based dosing of active vitamin D sterols were evaluated. When accounting for active vitamin D sterol administration, PTH in African-American and Hispanic subjects on HD was 28.8% (p=0.0002) and 17.5% (p=0.03) higher than in Caucasian patients on HD - findings consistent with those of the entire cohort. Secondly, in an analysis of the pediatric sub-group of patients (age less than 19 years, n = 302), African-American race and Hispanic ethnicity again predicted greater PTH levels across the first year of dialysis when compared to Caucasian race (45% higher in African-American, p=0.001, and 28% higher in Hispanic, p=0.01). Finally, within a sub-group of 167 patients with available 25-OHD levels (27% African-American, 35% Caucasian and 38% Hispanic) there was *no* significant difference in serum PTH across the first year of dialysis between racial-ethnic groups, a finding contrary to the analysis of the entire cohort. This sub-cohort of patients with available 25-OHD levels is notably smaller in size, more vitamin D sufficient and more likely to have been taking nutritional vitamin D supplementation than the overall cohort.

Discussion

This study describes differences in markers of MBM across racial-ethnic groups within a group of pediatric and young adult dialysis patients. Our findings of higher PTH levels in African-American children on dialysis are consistent with studies performed in both healthy children and adult dialysis patients [11–15]. Despite limited data on how Hispanic ethnicity impacts PTH levels, some data suggest lower PTH levels in Hispanics when compared to African-Americans; this is consistent with the current findings [15]. In our cohort, active vitamin D sterol administration did not account for racial-ethnic differences in PTH and it remains important to address the possible conclusion that African-American patients simply need a higher administered dose to achieve target PTH levels. Such a conclusion must be drawn with extreme caution given African-Americans have demonstrated unique differences in mineral and bone physiology. For instance, studies have demonstrated that the propensity toward higher PTH levels in African-Americans may be attributed to greater PTH fluctuations in response to stimuli such as hypocalcemia or to the noted higher parathyroid glandular mass on autopsy [22, 23]. Furthermore, there is evidence to suggest decreased sensitivity to PTH-induced resorption as a potential etiology for the preservation in bone density in African-Americans [24]. Additionally, it is critical to remember that for African-American adults on dialysis, low bone turnover is seen on histology at substantially higher PTH levels than that of Caucasian dialysis patients, and that African-Americans meeting prior KDOQI-defined goals for calcium-phosphate product and PTH have demonstrated a high prevalence of adynamic bone disease [11, 25]. Thus, these differences in PTH do not simply suggest the need for treatment with higher doses of active vitamin D amongst African-Americans and such a conclusion might promote development of low bone turnover amongst this population. However, these differences prompt the need for deeper insight into the role of self-reported race/ethnicity on PTH targets and ultimately the need to uncover better biomarkers to guide personalized treatment decisions.

Our findings further suggest that female gender modifies the relationship of race and serum PTH levels. Indeed, prior studies, such as a study by Harkness *et al.*, have demonstrated racial-ethnic differences in PTH using populations of African-American and Caucasian adolescent girls [2]. Paradoxically, despite higher PTH, the AP levels in our group of African-American patients, particularly African-American females, were consistently lower than those of Caucasian patients. The reason for this difference in our cohort is not clear and warrants further investigation to determine its reproducibility. Given low AP has been shown to be a good predictor of adynamic bone disease in African-American adults on dialysis, this finding may again underscore the potential toward low bone turnover in the African-American population even with PTH levels that are notably higher than their Caucasian counterparts [26]. Knowing that AP is affected by pubertal status, we must also consider whether or not differences in pubertal status, which are not considered in this analysis, partially mediate this finding [27]. Still, given that this finding persists even in the analysis of AP z-scores, it seems less likely to be solely attributable to pubertal status.

The current study additionally demonstrates differences in calcium and phosphate levels by race and ethnicity. Healthy African-Americans are known to have greater calcium and phosphate balance than Caucasians, likely owing to decreased fractional excretion of both calcium and phosphate [28–30]. Our findings show similar serum calcium and lower serum phosphate levels in African-Americans. Lower phosphate concentrations in African-American dialysis patients have previously been described in adults although adult findings remain conflicting [30–34]. A study in the pre-dialysis Chronic Renal Insufficiency Cohort (CRIC) demonstrated that *greater* serum phosphate was associated with African-American race as well as with lower income level, regardless of race [35]. This suggests a likely contribution of socioeconomic differences in dietary phosphate, a possibility that future studies must consider in the assessment of serum phosphate and PTH levels in relation to race and ethnicity.

This study is one of the first to explore mineral metabolism differences by race and ethnicity in children and young adult dialysis patients. Further studies are needed to investigate these differences thoroughly. A major strength of the current study is the use of a centralized laboratory, which makes the reported values reliable and allows for small differences to be more likely attributable to physiological behavior rather than laboratory variability. An additional strength of the current study is the national representation of patients which makes these results more likely to be reflective of the population at large given the inherent variability within the sample.

An important limitation of our study is in the definition of race and ethnicity; a variable often assessed using mutually exclusive racial categories and a single option for ethnicity. Race and ethnicity, as commonly defined, fail to account for nuances such as mixed racial lineage and differences in racial lineage within ethnic categories. For instance, our use of “Hispanic” as an ethnic category fails to reflect African ancestral descent in Puerto Rican American patients as opposed to Native American descent in Mexican American patients [36]. Furthermore, current racial-ethnic categories have evolved alongside societal pressures and are confounded by associations with socioeconomic status and other systemic barriers that might impact CKD-MBD adherence and treatment [36, 37]. Thus, a true understanding

of how CKD-MBD markers differ between racial-ethnic categories requires the consideration of true ancestral lineage in future studies. Such an approach would assist in isolating the contributions of specific genetic markers to CKD-MBD differences from the social context inherent to our current racial-ethnic categories.

Another limitation of our study is the lack of available data on serum 25-OHD. This is an important variable as it is known to be lower in African-American patients and could potentially act as a mediator of the higher PTH values when compared to Caucasian patients. Though studies in the general pediatric population show that 25-OHD inversely correlates with PTH values, African-American adults with CKD have shown a diminished correlation such that higher PTH occurs in African-Americans even after controlling for differences in 25-OHD [38]. Our sub-analysis of patients with available 25-OHD levels did not reveal a racial-ethnic difference in PTH levels although the ability to detect this difference may be limited by the small patient sample. In addition, the relationship of vitamin D and PTH remains quite complex, particularly as it applies to race and ethnicity. For instance, Powe *et al.* demonstrated that within strata of similar PTH levels, African-Americans have lower 25-OHD levels yet similar levels of bioavailable vitamin D in comparison to Caucasians [39]. This finding is thought to result from differences in vitamin D binding protein (VDBP) polymorphisms that result in differences in the level of bioavailable vitamin D. Therefore, the relationship of vitamin D and PTH by race and ethnicity is complex and deserves further studies that consider such polymorphisms in order to provide a more thorough evaluation.

We hypothesize that the higher levels of PTH among racial-ethnic minorities and differences in other MBM markers presented in our findings are reflective of a number of factors including: 1) underlying biological differences in the way bone responds to the perturbations of CKD-MBD, 2) the presence of social factors which contribute to differences in calcium and phosphate intake, and 3) differences in access to care/medications and medication adherence. Thus, future studies will need to consider the impact of ancestral informative markers on differences in bone and mineral markers with an effort to distinguish the role of ancestral lineage from the impact of socioeconomic circumstances related to the categories of race and ethnicity. Ultimately, the idealized approach to CKD-MBD care will jointly address the impact of genetics and socioeconomic risks on CKD-MBD outcomes, the former contributor being addressed by personalized treatment targets and the latter by increased access to appropriate foods, interventions to improve patient education and adherence, and increased access to care/medications.

In conclusion, the markers of MBM, which are critical to the clinical management of dialysis patients, show differences by race and ethnicity. We found that within a largely adolescent population, African-Americans and Hispanics on dialysis have higher PTH levels than Caucasians, and these findings are magnified in the female population. Future studies are needed to confirm these differences and their association with more accurately defined ancestral lineage with hopes of ultimately allowing a more personalized approach to CKD-MBD care.

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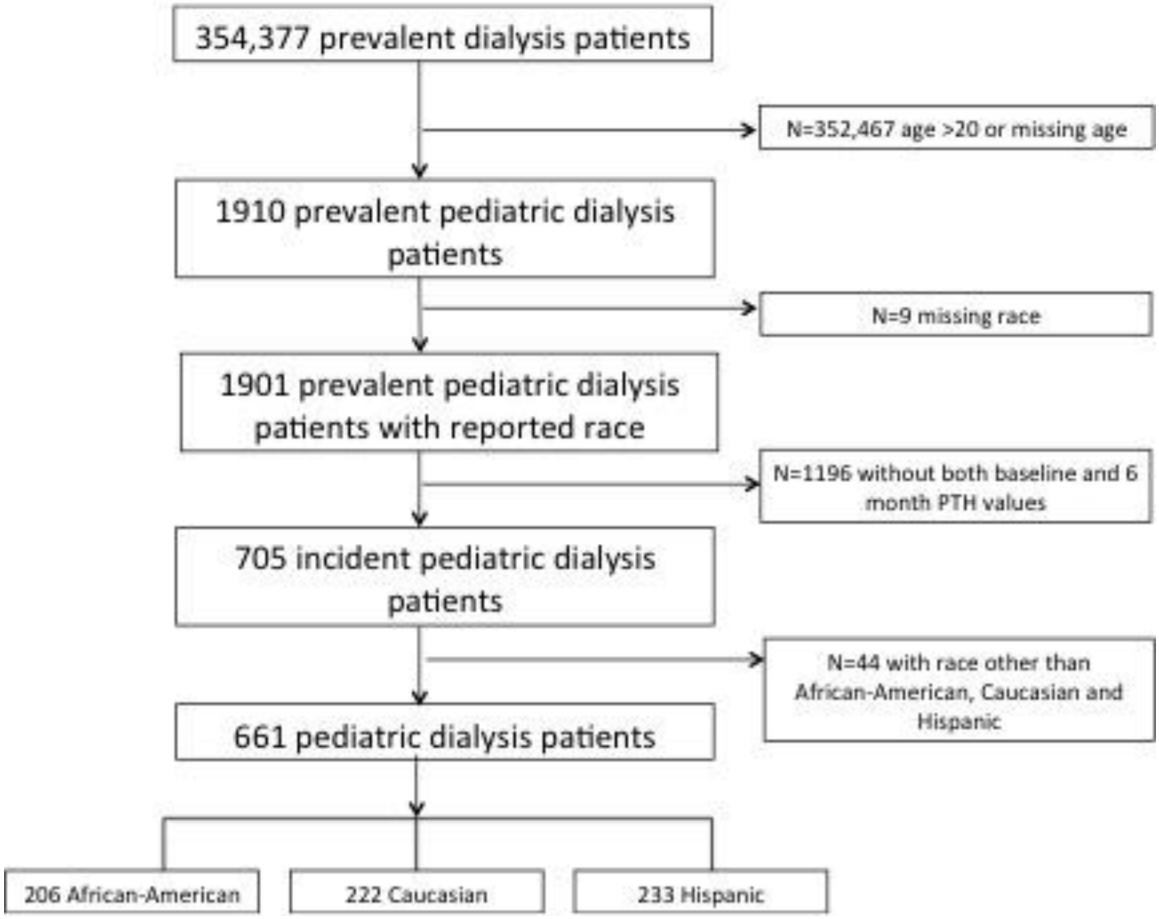

Fig 1.
Cohort Construction

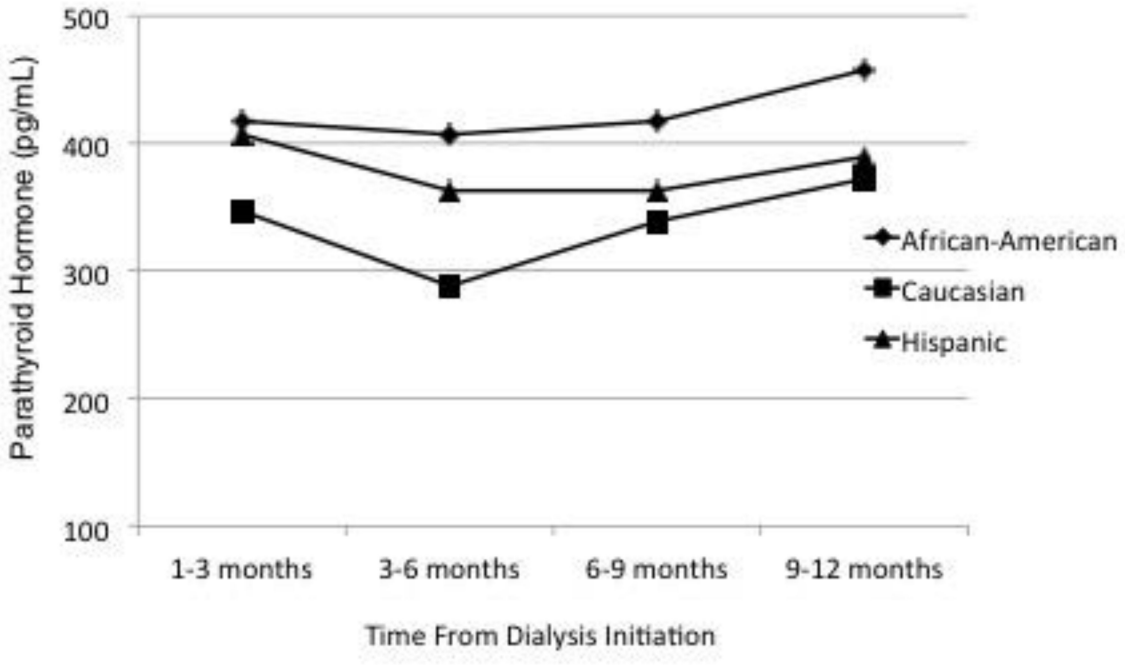

Fig 2.
Trend in Geometric Mean Parathyroid Hormone by Race and Ethnicity

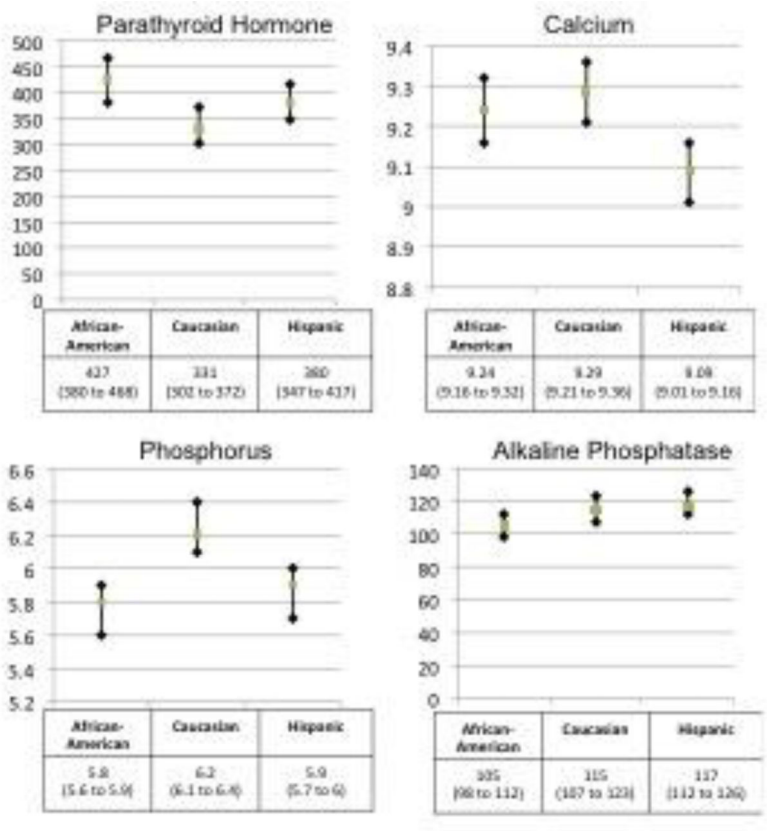

Fig 3.

Geometric Mean of mineral and bone metabolism (MBM) markers by Race and Ethnicity within the first year of dialysis

Table 1

Baseline demographic, laboratory and clinical characteristics of children and young adult patients stratified by race-ethnicity

Variable		Racial-Ethnic Group			
	Total	African-American	Caucasian	Hispanic	P values
N (%)	661	206 (31)	222 (34)	233 (35.2)	
Age, median (IQR)	19 (16–20)	19 (17–20)	19 (16–20)	18 (15–19)	0.001
Age Categories, n (%)					0.1
<6	31 (4.7)	4 (1.9)	14 (6.3)	13 (5.6)	
6–11	38 (5.7)	12 (5.8)	9 (4.1)	17 (7.3)	
12–18	233 (35.2)	63 (30.6)	75 (33.8)	95 (40.8)	
19–<21	359 (54.3)	127 (61.7)	124 (55.9)	108 (46.4)	
Male Gender, n (%)	361 (54.6)	104 (50.5)	128 (57.7)	129 (55.4)	0.3
Female Gender, n (%)	300 (45.4)	102 (49.5)	94 (42.3)	104 (44.6)	
Cause of ESRD, n (%)					0.001
CAKUT	87 (13.2)	21 (10.2)	41 (18.5)	25(10.7)	
GN	247 (37.4)	88 (42.7)	74 (33.3)	85 (36.5)	
Other/Unknown	327 (49.5)	97 (47.1)	107 (48.2)	123 (52.8)	
Initial Modality, n (%)					0.0002
Hemodialysis	502 (76.3)	175 (85.4)	167 (75.9)	160 (68.7)	
Peritoneal Dialysis	156 (23.7)	30 (14.6)	53 (24.1)	73 (31.3)	
Baseline Medications,n (%)					
Cinacalcet	64 (9.6)	14 (6.8)	31 (14)	19 (9.7)	0.03
Non Calcium Based Binder	323 (48.9)	92 (44.7)	107 (48.2)	124 (53.2)	0.2
Calcium Based Binder	346 (52.3)	106 (51.5)	118 (53.2)	122 (52.4)	0.9
Nutritional Vitamin D supplement	193 (29.2)	51 (24.8)	61 (27.5)	81 (34.8)	0.06
Baseline Laboratory measurements					
Calcium (mg/dL), mean ± SD	9.18 ± 0.68	9.19 ± 0.68	9.30 ± 0.66	9.06 ± 0.68	0.001
Phosphorus (mg/dL), mean ± SD	5.73 ± 1.43	5.59 ±1.46	5.89 ± 1.49	5.71 ± 1.34	0.09
Phosphorous z-score, median [IQR]	3.50 [1.74, 5.6]	3.31 [1.62,5.60]	3.92 [1.85,6.37]	3.31 [1.68,5.36]	0.2
Parathyroid Hormone (pg/mL), median [IQR]	410 [239,690]	411 [236,737]	368 [203,584]	471 [277,779]	0.005
Alkaline Phosphatase (IU/L), median [IQR]	92 [69,141]	82 [65,115]	90 [66,145]	105 [75,170]	<0.0001
Alkaline Phosphatase z-score, median [IQR]	−1.17 [−1.78, -0.07]	−1.28 [−1.79,-0.42]	−1.20 [−1.85, -0.04]	−0.98 [−1.72,0.31]	0.03

IQR: Interquartile Range

SD: standard deviation

ESRD: End Stage Renal Disease

CAKUT: Congenital Anomalies of the Kidney and Urinary Tract

GN: Glomerulonephritis

Table 2

Racial-ethnic differences in the markers of mineral and bone metabolism across the first year of dialysis [a]

	Racial-Ethnic Group (ref =Caucasian)	Percent and Mean Difference (95% CI)[b]	P value
PTH[c]	African-American	23% (4.7% to 41.3%)	0.01
	Hispanic	17.5% (2.3% to 38%)	0.02
Alkaline Phosphatase [d]	African-American	−8.8% (−14.9% to −0.9%)	0.03
	Hispanic	4.7% (−4.5% to 12.2%)	0.4
Calcium	African-American	−0.05 (−0.15 to 0.05)	0.4
	Hispanic	−0.2 (−0.3 to −0.11)	<0.0001
Phosphorous	African-American	−0.46 (−0.68 to −0.25)	<0.0001
	Hispanic	−0.34 (−0.56 to −0.13)	0.001

a. Adjusted for age, gender, race-ethnicity, ESRD etiology, Modality, Calcium, Phosphorus z-score, Alkaline Phosphatase z-score and cinacalcet use (in PTH and Calcium models). Interaction of race-ethnicity and time significant and included in PTH model only.

b. Percent difference for log transformed variables obtained by the following formula: [(10^B)-1]*100

c. Representative of log-transformed PTH

d. Representative of log-transformed AP

Table 3

Racial-ethnic differences in the markers of mineral and bone metabolism across the first year of dialysis, stratified by gender [a]

	RacialEthnic Group (ref= Caucasian)	Female		Male	
		Difference[b]	P value	Difference[b]	P value
PTH[c]	African-American	38% (14.8% to 69.8%)	0.001	4.7% (−12.9% to 28.8%)	0.6
	Hispanic	28.8% (4.7% to 54.9%)	0.01	4.7% (−12.9% to 25.9%)	0.6
Alkaline Phosphatase[d]	African-American	−10.9% (−20.6% to −0.7%)	0.04	−4.5% (−14.9% to 4.7%)	0.3
	Hispanic	−0.05% (−10.9% to 12.2%)	1	9.6% (−2.3% to 20.2%)	0.1
Calcium	African-American	−0.05 (−0.25 to 0.14)	0.6	−0.08 (−0.21 to 0.06)	0.3
	Hispanic	−0.26 (−0.46 to −0.07)	0.01	−0.18 (−0.31 to −0.06)	0.005
Phosphorous	African-American	−0.34 (−0.64 to −0.04)	0.03	−0.58 (−0.89 to −0.26)	0.0003
	Hispanic	−0.23 (−0.54 to 0.07)	0.1	−0.42 (−0.72 to −0.13)	0.01

[a] Adjusted for age, gender, race-ethnicity, ESRD etiology, Modality, Calcium, Phosphorus z-score, Alkaline Phosphatase z-score and cinacalcet use (in PTH and Calcium models). Interaction of race-ethnicity and time not significant in all models.

[b] Percent difference for log transformed variables obtained by the following formula: [(10^B)-1]*100

[c] Representative of log-transformed PTH

[d] Representative of log-transformed AP