Chronic Kidney Disease Is Under-Screened in SCD and Mild Albuminuria is Associated with a Drop in Hemoglobin: A Report from the GRNDaD Sickle Cell Registry

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Background

- The Globin Research Network for Data and Discovery (GRNDaD) is a combined effort from 6 US clinical sites that care for people with sickle cell disease (SCD)
- The goal is to improve care through shared data collection and review
- Here we report on 758 adults with SCD
- We reviewed adherence to the 2014 NHLBI Guidelines which recommends annual screening for albuminuria in anyone over age 10 with SCD

Objectives

- To review adherence to the NHLBI guidelines on albuminuria screening
- To analyze this data by patient genotype, sex, and hemoglobin levels

Methods

The Registry

- GRNDaD collects baseline and prospective annual updates via a single IRB-Reliant protocol, managed at Johns Hopkins
- Registry data is housed in a REDCap database
- Data is extracted manually from electronic health records at most sites. Automated data collection from EPIC occurs at one site (JHU) for approximately 60% of data points.

Analysis

- Of 758 adults in the registry, 411 had one or more annual follow up visits where data was collected, yielding 826 distinct observation years
- For this analysis subjects on chronic transfusions were excluded
- Subjects were stratified by genotype, with sickle cell anemia (SCA) defined as HbSS or HbSβ_0 thalassemia, and all other genotypes defined as "variant"
- Degree of albuminuria was graded into three groups: A1: none (<30mg), A2: albuminuria (30mg–300mg), A3: high grade albuminuria (>300mg)
- Statistics: multivariable linear mixed effects model, controlling for gender and age, with randomly varying intercept based on subject characteristics was used.

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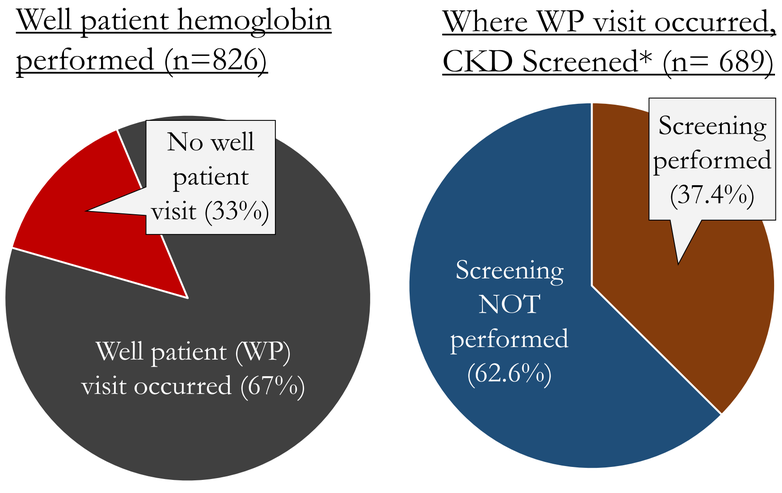
Table 1. Genotype

SCA Genotypes		Variants	
SS	267	SC	77
Sβ^0 Thalassemia	12	Sβ$^+$ Thalassemia	40
		Other	15
Total	279	Total	132

Table 2. Age & Gender

	All patients
Average Age [range]	38.3 [18-78] (n=411)
Female, %	240, 58.5%

Figure 1. Well patient follow up and albuminuria screening (observation years)



*Association between whether screened performed and site of care ($p<.0001$). Range of guideline adherence was 34.2% to 75.9% of observation years. No association between adherence and genotype or gender.

Table 3. Associations between Albuminuria and Hemoglobin

Degree of Albuminuria	Average Hemoglobin Relative to Subjects with no Albuminuria (A1)		Average Hemoglobin Relative to Subjects with no Albuminuria (A1) in those with Preserved Creatinine (<1mg/dL)	
	SCA Genotypes	Variants	SCA Genotypes	Variants
A1: No albuminuria (<30mg)	9.15 g/dL (n=59)	11.05 g/dL (n=69)	9.13 g/dL (n=51)	10.76 g/dL (n=56)
A2: Albuminuria (30mg–300mg)	–0.79* (n=52)	+0.33 (n=15)	–0.61* (n=42)	+0.04 (n=13)
A3: High grade albuminuria (>300mg)	–0.61 (n=20)	–1.86* (n=5)	–0.58 (n=11)	–1.90* (n=4)

* significant, $p < 0.05$

Conclusions

- A multisite, single IRB prospective registry is feasible in the contemporary American SCD population.
- Currently adherence to guideline based recommendations on assessments for CKD in established sickle cell centers in the US is poor.
- An added urgency to screening is suggested by the early association of albuminuria with worsening anemia, even in the absence of elevated creatinine
- These findings emphasize the importance of longitudinal cohorts such as the GRNDaD registry to help understand this relationship between anemia and the development of CKD, as well as how SCD progresses in adult patients

Limitations and Future Plans

- Some of the stratified groups, such as SCA genotypes with high grade albuminuria, had very small sample sizes
- The associations between hemoglobin and albuminuria identified in this study call for further research to elucidate causality and mechanisms behind them
- Strategies to assist providers with adherence to guideline based recommendations for routine screening for chronic kidney disease in adults with SCD are needed.