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POSTER ABSTRACTS

114.SICKLE CELL DISEASE, SICKLE CELL TRAIT AND OTHER HEMOGLOBINOPATHIES, EXCLUDING THALASSEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Neighborhood Disadvantage Increases Risk of Adverse Clinical Events in Children with Sickle Cell Disease

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Background: Hydroxyurea is the most widely used pharmacologic agent to treat patients with sickle cell disease (SCD). Hydroxyurea treatment has well established effects of inducing expression of fetal hemoglobin (HbF) and a beneficial impact on clinical outcomes such as reduced number of vaso-occlusive (VOC) events, transfusions, and hospitalizations. In non-SCD populations, living in socio-economic disadvantage is a well-established factor for poor health outcomes. However, there is a paucity of data to describe how social stressors impact children with SCD. We hypothesized that socio-economic disadvantage impacts risk of adverse clinical outcomes in pediatric SCD patients even while on hydroxyurea therapy.
Methods: We performed a retrospective chart review on 121 pediatric patients with severe SCD genotypes (homozygous HbS and sickle-beta ^{0} thalassemia) seen at Texas Children's Hospital (TCH) between 2010-2021. All patients were treated with hydroxyurea for a minimum of five years. Adherence to hydroxyurea was assessed through lab markers including absolute neutrophil count and reticulocyte counts. Patients not adherent were excluded from analysis. We examined the incidence of all clinical events for a total of 1026 patient years, including the number of office visits, ER visits, hospitalizations, transfusions, VOC, acute chest syndrome episodes (ACS), acute splenic sequestration (ASS), and febrile illness. We collected laboratory data including absolute neutrophil count, hemoglobin level, and HbF levels for each patient per year they were on hydroxyurea. We used the area deprivation index (ADI) to determine a score of neighborhood disadvantage amongst our cohort of patients. The ADI is a factor-based index which uses 17 US Census variables including poverty, education, and employment. We used individual residential addresses during our observation period to assign a geocode specific to each individual and obtain an ADI score. The ADI scores are ranked from 1-10, with higher ADI rankings reflecting a higher level of disadvantage.
Results: All individuals with SCD had a robust response to hydroxyurea within their first year of initiating the drug (>20% HbF). We stratified our cohort based on their ADI scores into low ADI (1-3; n=42); medium ADI (4-6; n=42); and high ADI groups (7-10; n=37), where high ADI is the group with highest levels of disadvantage. All three groups had a similar average duration of hydroxyurea treatment. There were no significant differences in age, sex, or reason given for starting hydroxyurea between the ADI groups. When we examined hydroxyurea response, there was no significant difference in HbF levels at 1 year (23.8 vs. 24.06 %HbF in the low vs. high ADI groups) or after 5 years (19.6 vs. 18.6 % HbF in the low and high ADI groups). Individuals with high ADI did started hydroxyurea at a younger age (2.9 years vs. 4.9 years, p=0.02). We found that any individual living in an area with higher ADI had an increased incidence of adverse clinical events. We calculated the incidence of each clinical event per 100 patient years in our 3 ADI groups and used a conditional maximum likelihood estimate of rate ratio method to compare incidences (Table 1). We found that among individuals living in an area with a higher ADI (more deprived region), there was increased frequency of ER visits, hospitalizations, transfusions, VOC, and ASS. In particular, patients with the highest ADI had a 3 and 5 times higher rate of VOC and ASS, respectively (Table 1).
Discussion: While we did not observe an association between ADI and HbF expression, our results show that higher neighborhood disadvantage is associated with poorer clinical outcomes among hydroxyurea-adherent pediatric patients with SCD who maintained a robust response to the drug (>20% HbF). All individuals in our study had a similar number of routine office visits at our clinic but any patient living in an area of high ADI had significantly more ER visits and hospitalizations for VOC and ASS events. While hydroxyurea is shown to reduce hospitalizations and VOC events in pediatric sickle cell patients, we show that neighborhood disadvantage can influence clinical outcomes even among patients who respond to hydroxyurea. More analysis remains in order to better characterize this association, and to understand additional strategies that can be used to reduce clinical events in pediatric patients of lower socioeconomic status.

Disclosures No relevant conflicts of interest to declare.

		Office Visits	ER Visits	Hospitalizations	Transfusions	VOC	ACS	ASS	Febrile
Low ADI (Score 1-3; n=42)	Incidence per 100 patient years	435.7	92.7	35.7	24.1	13.2	12.7	1.9	12.4
370 patient years	Rate	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Medium ADI (Score 4-6; n=42)	Incidence per 100 patient years	471	193	63.7	35.7	31.3	12.4	5.3	16.8
339 patient years	Rate	1.08	**2.08**	**1.79**	**1.48**	**2.36**	0.98	**2.81**	1.35
High ADI (Score 7-10; n=37)	Incidence per 100 patient years	520	156	79.2	36.9	40.1	17.7	9.8	18.6
317 patient years	Rate	1.19	**1.68**	**2.22**	**1.53**	**3.03**	1.39	**5.17**	1.49
	Significance	NS	**<0.0001**	**<0.0001**	**0.002**	**<0.0001**	NS	**<0.0001**	NS

Table 1. Comparison of adverse clinical events in SCD individuals based on ADI scores. We used the Area-Deprivation Index scores to categorize 121 SCD individuals into low, medium, and high ADI groups. We extracted clinical outcomes information for each individual for a minimum of 5 years while maintained on hydroxyurea treatment. For each ADI group, we estimated the incidence of each clinical event per 100 patient years. We used a conditional maximum likelihood estimate of rate ratio method to compare incidences between the three ADI groups (Rate) and provide statistical testing. NS means non-significant.

Figure 1

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