Depression among Privately Insured Children and Young Adults in the United States with Congenital Adrenal Hyperplasia

Lauren A Harasymiw[1], Scott D Grosse[2], Rebecca H Bitsko[2], Ruth Perou[2], Kathryn R Cullen[3], Kyriakie Sarafoglou[4]

[1] University of Minnesota Medical School, Department of Pediatrics, Minneapolis, MN, USA;
[2] National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, GA, USA;
[3] University of Minnesota Medical School, Department of Psychiatry and Behavioral Science, Minneapolis, MN, USA; [4] University of Minnesota Masonic Children's Hospital, Divisions of Pediatric Endocrinology and Genetics & Metabolism, Minneapolis, MN, USA

Introduction

- Congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency is characterized by impaired cortisol synthesis and *disruption in the hypothalamic pituitary adrenal (HPA) axis* leading to excessive adrenal androgen production (**Figure 1**) [1].
- Treatment requires *lifelong glucocorticoid replacement*.
- Patients with CAH fluctuate between *hypocortisolemic and hypercortisolemic states* over the course of the day due to the shortcomings of current therapy options.
- HPA axis dysfunction is strongly associated with major depressive disorder in adults, and studies have shown an association between *hypercortisolemia and depression* in children and adolescents [2].
- Little is known of the effect that HPA axis dysregulation has on depression in children and young adults with CAH.

The **objective** of the current study was to investigate the prevalence of depression in a large administrative sample of insured children and young adults with CAH as compared to their peers without CAH in the United States .

Figure 1. HPA axis function in CAH

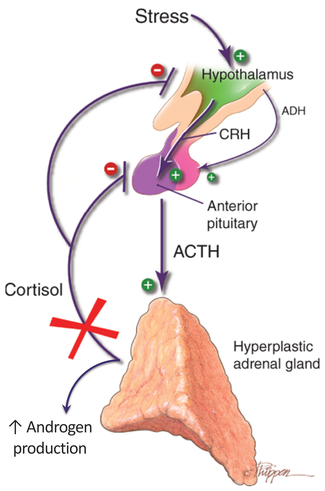


Image adapted from Sarafoglou K, Hoffmann GF, Roth KS. *Pediatric Endocrinology and Inborn Errors of Metabolism, 2e*; 2017

Methods

- We used the Treatment Pathways® interface to analyze health insurance claims data in the IBM® MarketScan® Commercial Databases.

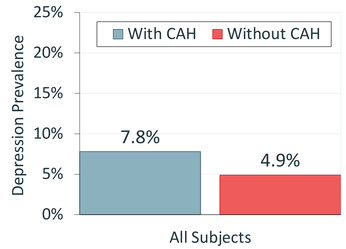
Figure 2. Study inclusion criteria

Enrolled in a participating private employer-sponsored insurance program → At least one claim between October 1, 2015 and July 31, 2020 → Between the ages of 4 and 25 years at first claim during study period

- Data from all individuals who met the inclusion criteria during the study period were included (**Figure 2**).
- **CAH prevalence** was measured as the percentage of subjects with ≥2 claims with the ICD-10 codes for CAH (E25.0) and ≥2 glucocorticoid prescriptions filled during the study period.
- **Depression prevalence** was measured as the percentage of subjects with ≥2 outpatient claims or 1 inpatient claim with an ICD-10 code for a depressive disorder within the relevant age group.

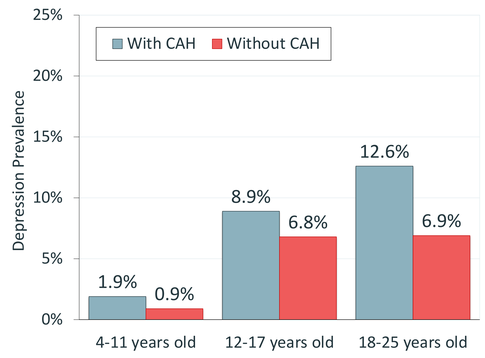
Results

- The study period prevalence of CAH was 1/11,660 (n=1,056).
- There was a higher unadjusted prevalence of depression among those with CAH (7.8%, n=82) as compared to their peers without CAH (4.9%, n=607,692).



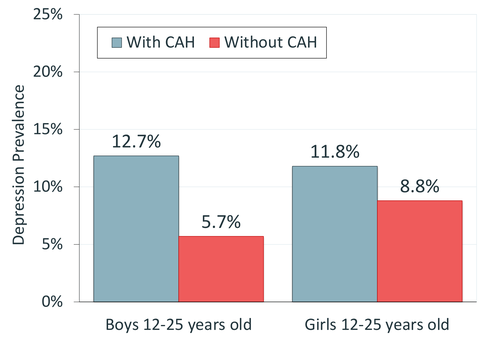
PR = 1.57, 95% CI: 1.28-1.94, p < 0.001

- After **stratifying by age group**, the prevalence of depression was higher across all ages among those with CAH as compared to those without CAH, however this difference only reached statistical significance in the older adolescent and young adult group (ages 18-25 years old).



	PR	95%CI	P-value
4-11	2.02	0.97-4.20	>0.05
12-17	1.34	0.93-1.89	>0.05
18-25	1.57	1.28-1.94	<0.001

- After **stratifying by gender among adolescents and young adults (12-25 years old)**, there was a significantly higher prevalence of depression among both boys and girls with CAH as compared to their peers without CAH.



	PR	95%CI	P-value
Boys	2.24	1.62-3.09	<0.001
Girls	1.34	1.04-1.74.	<0.05

Conclusions

- Several prior studies of children or adults with CAH have reported mixed results regarding the risk for depression [3-5].
- We used a *large administrative sample of privately insured children and young adults* in the United States to identify depression cases among those with and without CAH.
- Our study prevalence for CAH was comparable to other population studies in the United States [6-7].
- The prevalence of depression among the general population in our study was also similar to national survey-based studies in the United States [8].
- Our findings are also consistent with other studies that have found a *higher prevalence of depression among children and adults with chronic and life limiting medical conditions* [9].
- Our findings are limited by the smaller sample size of subjects who met criteria for CAH.
- *Enhanced screening for symptoms of depression* among the pediatric and young adult population with CAH in the United States might be warranted, if these associations are confirmed in further research.

Acknowledgments

- This research is supported by the National Institutes of Health's National Center for Advancing Translational Sciences, grant UL1TR002494. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health's National Center for Advancing Translational Sciences.
- Dr. Sarafoglou receives support from the DHHS FDA, NIH NCI, Spruce Biosciences, Alexion, Adrenas and Neurocrine.
- MarketScan® data are licensed by IBM® to the Centers for Disease Control and Prevention (CDC) for public health use by CDC researchers. The findings and conclusions in this report do not necessarily reflect the official position of the CDC.

References

1. Speiser PW, Arlt W, Auchus RJ, et al. Congenital Adrenal Hyperplasia Due to Steroid 21-Hydroxylase Deficiency: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2018;103(11):4043-4088.
2. Guerry JD, Hastings PD. In Search of Hpa Axis Dysregulation in Child and Adolescent Depression. Clin Child Fam Psychol Rev. 2011;14(2):135-160.
3. Idris AN, Chandran V, Syed Zakaria SZ, Rasat R. Behavioural Outcome in Children with Congenital Adrenal Hyperplasia: Experience of a Single Centre. Int J Endocrinol. 2014;2014:483718.
4. Messina V, Hirvikoski T, Karlsson L, et al. Good Overall Behavioural Adjustment in Children and Adolescents with Classic Congenital Adrenal Hyperplasia. Endocrine. 2020;68(2):427-437.
5. Jenkins-Jones S, Parviainen L, Porter J, et al. Poor Compliance and Increased Mortality, Depression and Healthcare Costs in Patients with Congenital Adrenal Hyperplasia. Eur J Endocrinol. 2018;178(4):309-320.
6. Therrell BL, Jr., Berenbaum SA, Manter-Kapanke V, et al. Results of Screening 1.9 Million Texas Newborns for 21-Hydroxylase-Deficient Congenital Adrenal Hyperplasia. Pediatrics. 1998;101(4 Pt 1):583-590.
7. Pearce M, DeMartino L, McMahon R, et al. Newborn Screening for Congenital Adrenal Hyperplasia in New York State. Mol Genet Metab Rep. 2016;7:1-7.
8. Ghandour RM, Sherman LJ, Vladutiu CJ, et al. Prevalence and Treatment of Depression, Anxiety, and Conduct Problems in Us Children. J Pediatr. 2019;206:256-267.e253.
9. Barker MM, Beresford B, Bland M, Fraser LK. Prevalence and Incidence of Anxiety and Depression among Children, Adolescents, and Young Adults with Life-Limiting Conditions: A Systematic Review and Meta-Analysis. JAMA Pediatr. 2019;173(9):835-844.

Contact Information

Lauren Harasymiw, MD, PhD, MPH, University of Minnesota, jelen009@umn.edu