

Pediatric Endocrinology

PEDIATRIC ENDOCRINOLOGY: ADRENAL, THYROID, AND GENETIC DISORDERS

Quality of Life in Children and Young People With Congenital Adrenal Hyperplasia in the United Kingdom - Nationwide Multicentre Assessment

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Introduction: Impaired Quality of Life (QoL) in Congenital Adrenal Hyperplasia (CAH) has been demonstrated in adults, but research in children has yielded variable results. We investigated the impact of CAH on QoL of children and adolescents alongside clinical health outcomes (biometric and biochemical profiles).

Method: We collected data from 14 tertiary UK centres to explore current health status of 8-18 year olds with CAH. QoL was assessed by using three different questionnaires; strengths and difficulties questionnaire (SDQ), Paediatric Quality of life (PedsQL) and Self-image profile (SIP), the former two completed by both patients and their parents. Height, weight and blood pressure were converted to age and sex adjusted z-scores. Serum markers included 17OH-progesterone (17OHP), androstenedione (D4), testosterone (T) and 11-ketotestosterone (11KT). **Statistical Analysis:** Statistical analysis comprised of principal component analysis (PCA) followed by multivariate analysis of variance (MANOVA), and post hoc regression. **Results:** Of the 107 CAH patients included in the study, median age 12.4 years (IQR 10.0-15.1), 55% were female and 104 completed at least 1 questionnaire. Adequate data for PCA was available from 73/107. Three Principal Components (PCs) with observed eigenvalues > 1 explained 71% of the total variance in the observed variables. PC1 reflected

'disease control' comprising 17OHP, D4, T and 11KT. PC2 reflected 'biometrics' comprising age, and height and weight z-score. PC3 reflected 'blood pressure', comprising systolic and diastolic z-score. PC1 correlated with outcomes in the parent and patient SDQ as well as parent PedsQL. PC2 and PC3 did not correlate with QoL. Regression analysis revealed higher scores (indicating lower QoL) in the SDQ domain of emotional problems and PedsQL domain of emotional health in patients where biomarkers suggested good control or overtreatment. Post hoc regression analysis revealed a rise in Androstenedione of 10nmol/L equated to an improved SDQ emotional problems score of 0.5 points and an improved PedsQL emotional health score of 3 points. **Conclusion:** The study found an interrelation between QoL and biomarkers of disease control in CAH. There were more emotional problems with higher levels of androgen suppression. Biochemical control within normal ranges did not predict emotional problems. However, unexpectedly, patients with very high levels of androgens were highlighted as reporting fewer problems with their emotional QoL. Further research into QoL in CAH and optimal levels of biochemical control will further understanding.

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Relationship Between Iodine Status and Thyroid Function in Preschool Children: From the Environmental and Development of Children (EDC) Study

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Background: We investigated iodine status and its association with thyroid function among preschool children residing in iodine-sufficient area. **Methods:** From the Environment and Development of Children study, 477 children were evaluated for thyroid function and urine iodine concentration (UIC) at age 6 during 2015-2017. After excluding children born with multiple birth and with congenital hypothyroidism or Hashimoto thyroiditis, 439 (231 boys) were included. Subclinical hypothyroidism (SCH) was defined as thyroid stimulating hormone (TSH) levels between 4.9-10 μ IU/mL with normal free T4 levels. Iodine status was evaluated by UIC and children were categorized into 4 groups: iodine deficient (UIC < 100 μ g/L), adequate (UIC, 100-299 μ g/L), mild excessive (UIC, 300-999 μ g/L), severe excessive (UIC \geq 1000 μ g/L). **Results:** Goiter was palpated in 64 (14.6%) with female predominance (26.0% vs. 4.3%, $P < 0.001$). Serum level of free T4 and T3 was 1.2 ± 0.1 ng/dL and 148.1 ± 18.5 ng/dL, respectively. The median TSH level was 2.3 (0.53-8.59) μ IU/mL and the

prevalence of SCH was 4.3% without sex-difference. The median UIC level was 606.2 (19.9-16409.7) $\mu\text{g/L}$, higher in boys (684 vs. 545 $\mu\text{g/L}$, $P = 0.021$) than in girls. Iodine was deficient in 19 (4.3%), adequate in 96 (21.9%), mild excessive in 170 (38.7%), and severe excessive in 145 (35.1%). After excluding 19 iodine deficient children, the relationship between iodine status and thyroid function was evaluated by multiple regression analysis after adjusting for age, sex, birth weight, gestational age, body mass index Z-score, and family history. As iodine status increased from adequate, mild excessive to severe excessive group, T3 levels decreased, and TSH levels increased with marginal significance (P for trend < 0.1 for T3 and TSH). When stratified by sex, similar association was found in only girls (P for trend = 0.043 for T3, and 0.062 for TSH) but not in boys, and mild excessive group showed lower free T4 levels ($\beta = -0.05$, $P = 0.013$) and severe excessive group had lower T3 levels ($\beta = -7.04$, $P = 0.035$) than iodine adequate group in only girls, but not in boys. **Conclusion:** Iodine was deficient in 4.3%, adequate in 21.9%, and excessive in 73.8% among preschool children residing in South Korea. As iodine status increased from adequate to excessive group, TSH levels increased with decreasing free T4 and T3 levels in girls.

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Risk of Complications in Children With Adrenal Insufficiency and Covid-19

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Background: Adrenal insufficiency may put a person at higher risk with infections due to a lack of normal stress response by the body. Limited data has been available in pediatric adrenal insufficiency with Covid-19 **Methods:** We used TriNetX, with a large COVID-19 database, collecting real-time electronic medical records data. We compared children (0-18 years) who were diagnosed with Covid-19 with and without Adrenal insufficiency. This database collected information from 54 health care organizations **Results:** Mortality rate in children with Covid-19 and Adrenal insufficiency was 2.246% (19/846). Mortality rate in children with Covid-19 without adrenal insufficiency was 0.097 % (244/252211). Relative risk of mortality for children with Covid-19 and Adrenal insufficiency was 23.2 with a p value of < 0.0001 . Endotracheal intubation rate in children with Covid-19 and Adrenal insufficiency was 1.418% (12/846). Endotracheal intubation rate in children with Covid-19 without Adrenal insufficiency was 0.065% (165/252211). Relative risk of endotracheal intubation for children with Covid-19 and Adrenal insufficiency was 21.68 with a p value of < 0.0001 . Sepsis rate in children with Covid-19 and Adrenal insufficiency was 6.974% (59/846). Sepsis rate in children with Covid-19 without Adrenal insufficiency was 0.274% (691/252211). Relative risk of sepsis for children with Covid-19 and Adrenal insufficiency was 25.45 with a p value of < 0.00001 . **Conclusion:** Mortality rate, endotracheal and sepsis showed increased association in children

with Adrenal insufficiency and Covid-19 versus children with Covid-19 and no Adrenal insufficiency. Further studies with larger sample size are needed to study complication rates of Covid-19 and Adrenal insufficiency.

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The Association of Insulin-Like Growth Factor-1 With Bone Mineral Density in Survivors of Childhood Acute Leukemia

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Background: The purpose of the current study is to investigate bone mineral deficit of children in survivors of childhood acute leukemia and examine the association of insulin-like growth factor-1 (IGF-1) with bone mineral density (BMD) status and the presence of osteoporosis. **Methods:** In a cross-sectional study of children diagnosed with different types of acute leukemia at age between 6 months and 18 years, serum IGF-1 and IGFBP-3, were assessed in relation to lumbar spine BMD (LSBMD) by using dual-energy x-ray absorptiometry and non-traumatic vertebral fracture by lateral thoracolumbar spine radiographs. Standard deviation scores (SDS) were calculated based on the age- and gender-adjusted population mean. **Results:** Among 189 children after completion of acute leukemia treatment, 22 (11.6%) children had LSBMD SDS less than -2.0 while 80 (42.3 %) children were diagnosed with osteoporosis. Mean areal BMD and LSBMD SDS of the subjects were $0.862 \pm 0.197 \text{ g/cm}^2$ and -0.6 ± 1.6 , respectively. IGF-1 and IGFBP-3 were lower in children with LSBMD lower than -2.0 ($P < 0.05$) and those with osteoporosis ($P < 0.05$). LSBMD SDS showed linear correlation with serum IGF-1 ($P = 0.041$). Low serum IGF-1 level ($OR = 0.724$, $P = 0.042$) and elder age of leukemia diagnosis ($OR = 1.089$, $P = 0.023$) were suggested risk factor of the occurrence of osteoporosis. **Conclusions:** Substantial number of survivors from childhood acute leukemia undergo bone mineral deficits, and serum IGF-1 status could be a prognostic factor associated with bone mass acquisition and future occurrence of osteoporosis.

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The Effects of Conditioning Regimen on Thyroid Function After Hematopoietic Stem Cell Transplantation in Children: 2-Year Short Term Follow Up

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