patients with idiopathic late-onset or metabolically-related AHH from this analysis. Testicular volume (TV), serum gonadotropins, total and bioavailable testosterone (TT and BT), estradiol (E2) and testicular peptides inhibin B (IB), AMH and INSL3 were measured at a single center in the absence of any hormone replacement. **Results**. TV was greater in patients with AHH (16.2±6.3 mL) than in those with CHH (3.4±2.7 mL; p<0.0001). Testicular hypotrophy (mean TV<12 mL) was found in 30% of patients with AHH and in 97% of those with CHH (p<0.0001). When adjusted for age and BMI, men with AHH still had a larger mean TV than those with CHH (p<0.0001). Cryptorchidism was more frequent in patients with CHH than in those with AHH (20.4 vs 0.2%, p<0.0001). Micropenis was found exclusively in patients with CHH. TT levels were higher in patients with AHH (1.4±0.9 ng/mL) than in those with CHH (0.4±0.3 mL, p<0.0001). LH, FSH, BT and E2 were higher in patients with AHH than in those with CHH (p<0.0001 for all parameters), as were IB and INSL3 levels (126±87 vs 59±55 pg/mL, and 566±372 vs 60±40 pg/mL, respectively, p<0.001). In contrast, serum AMH and SHBG levels were lower in patients with AHH than in those with CHH (246±234 vs 46±38 pmol/L, and 35±22 vs 26±21 nmol/L, respectively, p<0.0001). Comparing hormone characteristics across different AHH subgroups, patients with craniopharyngioma (n=44) had lower TV (7.7±5.3 mL) and lower TT, BT, E2, IB and INSL3 levels than those with AHH caused by any other etiology (p<0.05 for all parameters). **Conclusions**. Our data demonstrate distinct profiles of clinical presentation and reproductive hormones between CHH and AHH. Clinical and hormonal impairment is more severe in patients with CHH than in those with AHH. Preservation of the gonadotrope/testicular axis activity during the fetal, neonatal and pubertal periods in patients with AHH likely accounts for these differences. Among AHH etiologies, patients with craniopharyngioma have the most severe impairment, likely as a result of the intrinsic severity of these tumors, the age at onset, and/or the aggressiveness of the available therapeutic procedures.

Reproductive Endocrinology

CHALLENGES IN REPRODUCTIVE ENDOCRINOLOGY: LATE BREAKING INSIGHTS

Distinctive Neuroendocrine Changes and Menstrual Dysfunction in Early Postmenarchal Daughters of Women With PCOS

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PCOS is a complex genetic disease with strong familial aggregation - ~40% of reproductive-age sisters have elevated testosterone (T) levels and other features of the syndrome. Beginning in infancy, daughters of affected women (PCOS-d) have elevated anti-Müllerian hormone (AMH) levels and evidence for global increases in 5α-reductase activity. Peripubertally, PCOS-d have increased T levels. Peripubertal overweight and obesity (OB) girls also have elevated T but not AMH levels.

We initiated a prospective study of PCOS-d and OB to test the hypothesis that only PCOS-d are at increased risk to develop PCOS. Herein, we present the baseline assessments in 14 PCOS-d, 14 OB, and 18 lean control girls (LC) aged 11-16 yrs who were enrolled within 2-yrs of menarche. PCOS-d mothers fulfilled NIH criteria, OB and LC mothers had no history of irregular menses or clinical hyperandrogenism. Morning blood sampling was performed for hormone levels. Free T was calculated from total T and SHBG. Ovarian MRI was performed to assess morphology. Data are mean ± SD, α=0.05.

By design, age did not differ between the groups, but BMI z-score was higher in OB compared with PCOS-d and LC (1.3±1.1 PCOS-d v 2.0±0.6 OB v 0.1±0.7 LC, P<0.0001). The prevalence of irregular menses (cycles ≤ 21d or ≥ 45d apart) was significantly increased only in PCOS-d (61% PCOS-d, 23% OB, 19% LC, X^2 P=0.03). Total T levels did not differ between the groups. SHBG levels were decreased in PCOS-d and OB (23±16 PCOS-d v 30±16 OB v 56±15 LC, nmol/L, P<0.0001), resulting in a trend toward increased free T levels in these groups (0.6±0.3 PCOS-d v 0.6±0.5 OB v 0.4±0.2 LC, ng/dL, P=0.06). DHEAS levels were higher in PCOS-d and OB compared with LC (135±35 PCOS-d v 150±68 OB v 88±46 LC, ug/dL, P=0.05). AMH levels, follicle counts and ovarian volume did not differ.

GnRH analog (GnRHa,10 μg/kg SC) stimulation was performed in 9 PCOS-d and 13 OB. Both baseline LH levels (7.6±4.4 PCOS-d v 3.7±2.1 OB, mIU/mL, P=0.01) and LH responses to GnRHa were significantly increased in PCOS-d (LH AUC: 2110±1132 PCOS-d v 1047±808 OB, P=0.01). Baseline FSH and FSH AUC did not differ. Post-GnRHa 17-OHP levels did not differ.

Early postmenarchal PCOS-d but not OB have evidence for increased GnRH-mediated LH release, a cardinal feature of PCOS disordered gonadotropin secretion. The increased prevalence of irregular menses in PCOS-d is consistent with this change. In contrast, androgen levels are similarly increased in both groups. These findings align with genomewide association studies implicating gonadotropin secretion and action in PCOS pathogenesis and suggest that neuroendocrine alternations in gonadotropin release are a core causal pathway in PCOS. Moreover, these findings provide further support for our hypothesis that PCOS-d but not OB are at increased risk for PCOS. Longitudinal studies are ongoing to test this hypothesis at 2-yrs postmenarche when the diagnosis of PCOS can be established.

Reproductive Endocrinology

HYPERANDROGENISM

Characterization of PCOS Among Flo App Users Around the World

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SUN-LB6

Polycystic ovary syndrome (PCOS) is a common gynecological endocrine disorder associated with menstrual irregularity and androgen excess. The worldwide prevalence of PCOS among women of reproductive age ranges from 5-20%. Mobile menstrual cycle apps, such as Flo, provide an opportunity to gather data on the characteristics of PCOS in a globally representative and medically unbiased population. The objective of this study was to report PCOS symptomatology relative to country in order to better characterize PCOS and its differing phenotypes among users around the world. A questionnaire on PCOS related symptoms and previous PCOS diagnosis was available to Flo users during one month (2019). The geographical location of the user was estimated based on the IP address. Study inclusion criteria included women aged 18-44 years seeking to track their cycle or to conceive, who were not pregnant, on active contraception, or in stabilization mode after pregnancy and had Flo app running in English. All users in the study had agreed to the use of their de-identified and aggregated data for research purposes.The highest number of Flo app users who completed the PCOS questionnaire were coming from the following top 5 countries: United States (US) (n=240,732), United Kingdom (UK) (n=67,696), India (n=40,171), the Philippines (n=35,097), and Australia (n=28,946). The percentage of self-reported PCOS in these countries was 14.4% with higher percentages in India, the Philippines, and Australia (22.6%, 20.0%, 15.9, respectively) and lower in the US and UK (12.2% and 13.71%, respectively). In the US, UK, and Australia, the most common self-reported symptoms of PCOS positive women were bloating, hirsutism, and irregular cycles. In India and the Philippines, the most common symptoms of women with PCOS were bloating, baldness, and irregular cycles. Hirsutism, high glucose and high levels of both cholesterol and glucose are the three top symptoms increasing the probability of PCOS in all studied countries. The percentage of self-reported PCOS increases 3.04 times among users that reported hirsutism compared to all users that positively responded to the PCOS self-assessment question. Probability of PCOS among users that report hirsutism increases 3.85 times for Australia and 4.24 times for India. Australia and India had higher percentages of self-reported PCOS among those who reported experiencing nearly all PCOS related symptoms. Using Flo's software, we are able to determine that geographic location has an effect on the phenotypic presentation of PCOS. Understanding the distribution of PCOS symptomology around the world will help to better characterize PCOS and improve diagnosis and treatment on both an individual and global scale.

Pediatric Endocrinology

PEDIATRIC OBESITY, THYROID, AND CANCER

Tyrosine Kinase Inhibitor Induced Hypothyroidism in Pediatric and Young Adult Population: An Institutional Review

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Tyrosine Kinase Inhibitor Induced Hypothyroidism in Pediatric and Young Adult Population: An institutional review**Background:**Tyrosine kinase inhibitors (TKIs) are a class of molecular targeted therapies approved for the treatment of several hematological and solid tumors in pediatric population. Thyroid dysfunction, most commonly primary hypothyroidism, is a well described adverse effect in adults. There is no available data in the pediatric population regarding the risk of thyroid dysfunction with the use of TKIs.**Objective:**To document the incidence of hypothyroidism in the pediatric and young adult patients on TKI therapy.**Methods:**A retrospective chart review including patients' ≤ 21 years of age who had been treated with at least 1 of 10 predetermined TKIs for malignancy was performed. Demographics, TKI use and duration, thyroid hormone labs, and history of head/neck radiation were collected. We excluded patients with pre-existing thyroid disease prior to start of TKI therapy. Thyroid dysfunction was defined as TSH >5mcIU/mL during TKI therapy. **Results:**A total of 152 patients who were treated with TKIs for malignancy were identified. The mean age was 12.4 years (SD 6.5). About 20% of patients had therapy with multiple TKI drugs. A total of 24 patients were noted to have TSH elevation >5mcIU/ml of which 19 had a TSH >10 mcIU/mL or low free T4. Fourteen patients were started on levothyroxine. Average duration of TKI therapy prior to development of thyroid dysfunction was 6.7 months but over half developed hypothyroidism within 3 months of initiation of TKI therapy. Cabozantinib and pazopanib were responsible for 70% of TKI associated cases of thyroid dysfunction.**Conclusion:**This is the first report of incidence of primary hypothyroidism in pediatric and young adult patients treated with TKIs. Thyroid dysfunction can develop in the first few months of therapy and often is clinically significant. Early recognition and treatment of this complication will be important for patient care especially as use of these class of drugs increase.

Reproductive Endocrinology

HYPERANDROGENISM

Relationship Between BMI and PCOS Symptoms Among Flo App Users in the United States

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SUN-LB3

Polycystic ovary syndrome (PCOS) is known to affect 6%-12% of women of reproductive age in the United States. PCOS is a heterogeneous condition associated with menstrual cycle irregularity and androgen excess. Though many women with PCOS have a BMI classified as overweight or obese, information is limited on how specific symptoms and BMI mediate PCOS diagnoses in the general population. A questionnaire on PCOS-related symptoms and previous PCOS diagnosis was available to Flo users