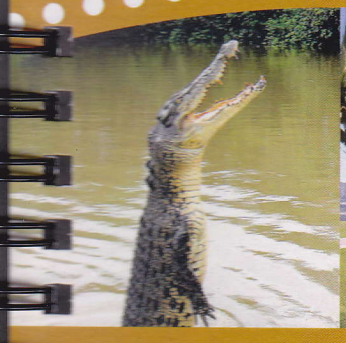
APPES & APEG JOINT MEETING

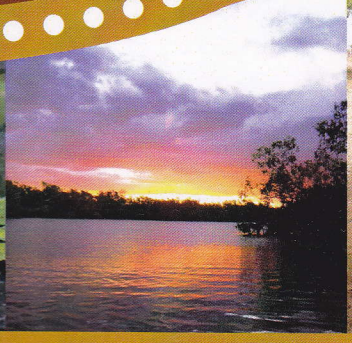
29 OCT - 01 NOV 2014

DARWIN, AUSTRALIA

APPES
ASIA PACIFIC PAEDIATRIC ENDOCRINE SOCIETY

Australasian Paediatric Endocrine Group




CONFERENCE ABSTRACT BOOK

1418 OR05.05
The outcomes of a standardized approach to managing metabolic bone disease of prematurity
LIT KIM CHIN, VIC, Australia

1418 OR06.05
Gender change and stigmatization in late-treated Indonesian children, adolescent, and adult patients with DSD
ANNASTASIA EDIATI, Indonesia

1430 [S6] SYMPOSIA: HOT TOPICS — Auditorium 2, Ground Floor
Chairs: Michelle Jack & Byung-Kuy Suh

1430 ***Dissecting congenital hypothyroidism by next generation sequencing***
SATOSHI NARUMI, Japan

1500 ***Insights into the diagnosis and management of congenital hypothyroidism***
PAUL HOFMAN, New Zealand

1530 Closing Ceremony — Auditorium 2, Ground Floor

*PRACTICAL STREAM
The practical stream is a series of concurrent sessions that are designed to be more interactive, hands on style sessions. The topics covered in this stream are designed for allied health staff such as educators, nurses, social workers, dietitians and also general paediatricians.

Program correct at the time of print and subject to change.

[1] *Institute of Endocrinology and Diabetes, The Children's Hospital Westmead*
[2] *Discipline of Paediatrics and Child Health, University of Sydney*

Turner syndrome (TS) and related sex chromosome abnormalities are associated with a variety of karyotypes and phenotypes affecting 1 in 2500 live births. Mosaicism with Y material (45,X/46,XY) and female phenotype is rare (<1 in 15 000 births)(1). Their risk of gonadal malignancy is 10-15%, and up to 50% in those with ambiguous phenotype at birth(2). The SHOX gene is located on both X and Y chromosomes but is more prone to deletions on the X chromosome, potentially influencing height outcomes across TS karyotypes(3). However, children with SHOX deficiency respond similarly to TS girls when treated with the same dose of growth hormone (GH)(4). We therefore examined height outcomes and gonadal malignancy rates in TS vs 45,X/46,XY females.

We identified 198 females aged ≤ 30 years with TS or mixed gonadal dysgenesis treated with GH (under TS or auxological criteria). Final height (FH) was available on 51 TS (45,X or mosaic without Y material) females. An additional 13 had 45,X/46,XY karyotype with TS phenotype, and two had non-mosaic 46,XY karyotypes with cytogenetic abnormalities consistent with TS. Of these 15 females, gonadal tissue histology was available for 11 and FH in nine. We evaluated patient records for age, height, mid-parental height (MPH), GH dose at commencement, duration of therapy and growth response at 12 months and at FH. Comparisons between TS and 45,X/46,XY groups were performed using the Mann-Whitney U test.

All 45,X/46,XY patients had a female phenotype and five had clitoromegaly at birth. Three were identified prenatally; age at diagnosis ranged from birth to 13 years, with the most common presenting features being short stature (n=5), ambiguous genitalia (n=5) and dysmorphic features (n=2). Of the 11 that underwent gonadectomy, four (none virilised at birth) had a gonadoblastoma, including one dysgerminoma in situ.

Age, height, MPH,GH dose at commencement, duration of therapy and height z-score after 12 months did not differ between groups. Median FH z-score for 45,X/46,XY was higher than TS, -1.12 [range -1.96,0.31], vs -1.59 [-3.12,0.01], p=0.016. Response to GH therapy (median Δ height z-score) after 12 months was similar: 0.45 [-0.04,0.84] vs 0.39 [-0.21,1.14], p=0.81. However, height response over the total duration of therapy was better for 45,X/46XY: 1.5 [0.72,2.88] vs 0.87 [-0.98,2.14], p=0.009.

45,X/46,XY females appear to respond differently to GH therapy, suggesting a possible contribution of SHOX on the Y chromosome. The rate of germ cell tumours in non-virilised females (36%) is higher than previously reported.

References:

1. Johansen ML, Hagen CP, Rajpert-De Meyts E et al. 45,X/46,XY Mosaicism: Phenotypic Characteristics, Growth, and Reproductive Function – a Retrospective Longitudinal Study. J Clin Endocrin Metab 2012; 97(8):E1540-1549.
2. Cools M, Pleskacova J, Stoop H, et al. Gonadal Pathology and Tumor Risk in Relation to Clinical Characteristics in Patients with 45,X/46,XY Mosaicism. J Clin Endocrin Metab 2011; 96(7): E1171-E1180.
3. Oliveira CS, Alves C. The role of the SHOX gene in the pathophysiology of Turner syndrome. Endocrinol Nutr 2011; 58(8): 433-442.
4. Blum WF, Ross JL, Zimmermann AG et al. GH Treatment to Final Height Produces Similar Height Gains in Patients with SHOX Deficiency and Turner Syndrome: Results of a Multicenter Trial. J Clin Endocrin Metab 2013; 98(8): E1383-1392.

OR06.04

CLINICAL AND MUTATIONAL SPECTRUM OF PATIENTS WITH CONGENITAL LIPOID ADRENAL HYPERPLASIA IN SOUTHEAST ASIA

Ariyawatkul, Kansuda[1], Jaruratanasirikul Somchit[2], Loke, Kah Yin[3], Nakavachara, Pairunyar[4], Kongkanka, Chawkaew[5], Sahakitrungruang, Taninee[1*]

[1] *Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, 10330*
[2] *Department of Pediatrics, Prince of Songkla University, Songkhla, Thailand*
[3] *Department of Pediatrics, KTP- National University Children's Medical Institute, National University Hospital, Singapore*
[4] *Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*
[5] *Queen Sirikit National Institute of Child Health, Bangkok, Thailand*

*Corresponding Author (Taninee.P@chula.ac.th)

Aims: Mutations in Steroidogenic Acute Regulatory protein (*StAR*) cause congenital lipoid adrenal hyperplasia (lipoid CAH), characterized by absent steroidogenesis, potentially lethal salt loss, 46,XY sex reversal and massively enlarged adrenals engorged with cholesterol esters. Nonclassic lipoid CAH is a recently recognized disorder caused by *StAR* mutations that retain partial function. We aim to delineate the clinical and mutational spectrum of *StAR* mutations in patients with lipoid CAH.

Methods: The entire coding regions of the *StAR* gene were assessed by polymerase chain reaction and sequencing analysis.

Results: There were 10 patients of lipoid CAH had mutations in the *StAR* gene with 5 novel mutations (p.P230L>WfsX, IVS6-1G>A, IVS3+(2-3)insT, p.W147R, p.Q264R). Eight patients had classic lipoid CAH presenting with adrenal crisis during early infancy (range of onset 3-11 months of age). Two siblings had nonclassic phenotypes with later onset adrenal insufficiency without disordered sex development. Adrenal enlargement by imaging was demonstrated in only 3 cases of classic lipoid CAH. The functional studies of novel StAR mutations are being under investigation.

Conclusion: *StAR* mutations may not be rare in Southeast Asian population. There is a broad clinical spectrum of *StAR* mutations varying from early onset adrenal insufficiency to late onset of glucocorticoid deficiency with only mild defects in mineralocorticoid and sex steroid synthesis. Adrenal gland enlargement is not pathognomonic for lipoid CAH.

OR06.05

GENDER CHANGE AND STIGMATIZATION IN LATE-TREATED INDONESIAN CHILDREN, ADOLESCENT, AND ADULT PATIENTS WITH DSD

Ediati, Annastasia[1,2], Juniarto, Achmad Zulfa[2], Birnie, Erwin[3], Okkerse, Jolanda[4], de la Croix, Anne[4], Wisniewski, Amy[5],Drop, Stenvert[4], Faradz, Sultana MH[2], Dessens, Arianne[4]

[1] *Diponegoro University, Faculty of Psychology, Semarang, Indonesia*
[2] *Diponegoro University, Faculty of Medicine, Center for Biomedical Research (CEBIOR), Indonesia*
[3] *Erasmus University Rotterdam – Institute of Health Policy and Management, the Netherlands*
[4] *Sophia Children's Hospital - ErasmusMC Rotterdam, the Netherlands*
[5] *University of Oklahoma Health Sciences Center, Oklahoma, United States*

In Indonesia clinical management of DSD is challenged by limited knowledge and limited diagnostic and treatment facilities. Prior to this study, most patients remained untreated and grew up with ambiguous bodies and doubts about their gender. We investigated patients' experiences of being raised in ambiguity.

118 Indonesian patients, ages 6 – 41, with 46XX DSD (n=27), 46XY DSD (n=77) and chromosomal DSD (n=14) were compared to 118 control subjects matched for gender, age, and living area. Questionnaires for gender identity, gender role behavior and social stigmatization were translated or designed. The psychometric properties were satisfactory. For patient and control group comparisons, Mann-Whitney U and Fisher's Exact tests were applied.

The results showed that 7% of the children, 8% of the adolescents and 44% of the adults changed gender, particularly non-diagnosed and non-treated patients with 46XY DSD (81%). 95% of the patients changed gender from female to male, including untreated patients with 46,XX CAH-SV. Compared to control groups, cross-gender role behavior was seen in young girls with 46XX CAH-SV ($p=.047$) and adolescent girls with different types of DSD ($p=.01$). In girls with DSD, confusion with gender identity was seen (young girls $p=.004$; adolescent girls $p=.01$). Adult men reported past cross-gender role behavior ($p=.01$) and past problems in gender identification ($p=.01$) prior to female-to-male gender change.

Children with genital ambiguity ($p<.006$) and cross gender behavior ($p<0.001$) and adults with ambiguous bodies ($p=.001$) and adults who changed gender ($p<0.03$) suffered stigmatization. Rejection or isolation elicited depression and withdrawal from social activities in girls ($p=.002$) and women ($p=.009$) and youngsters who had changed gender ($p=.02$).

We conclude that high percentage of our patients changed gender. The wish for gender change was particularly seen in patients with progressive masculinization. Patients with DSD who had visible ambiguity in physical and behavioral appearance suffered stigmatization. Teasing and rejection led to strong emotional reactions. Early clinical evaluation and treatment, patient and parent education, and teaching coping strategies will improve quality of life.