

# British Society for Paediatric Endocrinology & Diabetes/British Paediatric and Adolescent Bone Group

## G93 THE OUTCOME OF PRENATAL IDENTIFICATION OF A SEX CHROMOSOME ABNORMALITY

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**Introduction** Prenatal diagnosis (PND) via amniocentesis or chorionic villus sampling may result in the identification of a sex chromosome abnormality, often as an incidental finding.

**Aims** To ascertain the incidence of sex chromosome abnormalities detected by prenatal diagnosis in the Grampian and the West of Scotland (WoS) regions and to determine the characteristics and outcomes of these cases.

**Methods** Retrospective review of all cases of prenatal diagnoses that revealed a sex chromosome abnormality between 2000 and 2012.

**Results** Over the period of 12 years, 166 positive cases were identified. The indication for PND was an abnormal ultrasound scan in 95(57%), high-risk first trimester screening results in 31(19%), age related aneuploidy risk in 24(14%), maternal anxiety in 9(5%) and a family history of a chromosomal abnormality in 7(4%). Of the 166 cases, 79(48%) cases were 45, X, 24(14%) were 47, XXY, 14(8%) were 48, XXX, 9(5%) were 45, X/46, XX,, 8(5%) had a structurally abnormal X chromosome, 7(4%) were 45X/46XY, 6(4%) were 48, XYY, 2(1%) were 46, XX/46XY and 17(11%) had other variations of sex chromosomes. Of the 166, 73(44%) pregnancies were terminated and of these cases, 47(64%) had a karyotype of 45, X. An additional 7 pregnancies(4%) were associated with an intrauterine death and 5 of these were 45, X. Based on a combined birth rate of 40,000 births per year for these regions, it is estimated that there was one positive case for 3,500 births and approximately half of these led to a live birth.

**Conclusions** 1:7000 births are associated with a prenatally diagnosed sex chromosome abnormality. 45, X is the most commonly encountered abnormality. Given the rare incidence, there is a need to improve our understanding of the care of these cases during the pregnancy as well as afterwards.

## G94 CHARACTERISING CHANGES IN THE IN VIVO RODENT BRAIN USING MAGNETIC RESONANCE SPECTROSCOPY

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**Background** By providing a non-invasive, functional insight, Magnetic Resonance Spectroscopy (MRS) has the potential to provide objective longitudinal data on mammalian brain development.

**Aim** To assess the sexual dimorphism in rodent brain chemistry and development using *in vivo* MRS.

**Methods** 26(19 male) Sprague-Dawley rats were scanned at 6wks and 20(16 male) at 10wks using a 7TMRI scanner. Testosterone concentrations were measured by ELISA. Metabolites were expressed as a ratio to creatine and full width at half-maximum (FWHM) of the water peak was used as a guide to the reliability of the ratios.

**Results** Median weight in 6wk males (M6) and females (F6), 10wk males (M10) and females (F10) was 197g(range,142–230), 131g (121–135), 316g(274–365) and 206g(191–210) respectively. Median anogenital distance (AGD) in M6, F6, M10, F10 was 2.46cm (1.89–2.9), 1.17cm(1.04–1.19), 3.25cm(2.8–3.6) and 1.33cm(1.07–1.60). Median serum testosterone in M6 and M10 were 1.33ng/ml (0.23–5.45) and 3.36ng/ml(1.75–8.26). 14 metabolites were identified in the occipitofrontal cortex. FWHM range was within the optimal range at 12–38Hz. In M6, myo-inositol ratios showed a positive association with circulating testosterone ( $p = 0.04$ ), and AGD was correlated with phosphocreatine ( $p = 0.033$ ) and glutamate ( $p = 0.045$ ). There was a difference between M6 and F6 in 3 metabolite ratios: phosphocholine ( $p = 0.014$ ), lactate ( $p = 0.046$ ) and NAA ( $p = 0.005$ ). In addition, in males, there was an increase from 6wks to 10wks in 3 metabolite ratios: taurine ( $p = 0.025$ ), myo-inositol ( $p = 0.012$ ) and phosphocholine ( $p = 0.005$ ).

**Conclusions** MRS is a reliable tool for studying the brain in maturing rats and may be a useful tool for studying the link between longitudinal changes in sex steroids and brain development.

## G95 ENDOCRINE LATE-EFFECTS POST-HAEMATOPOIETIC STEM CELL TRANSPLANT(HSCT) IN CHILDREN WITH HAEMOGLOBINOPATHIES

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Children with haemoglobinopathies undergoing HSCT are not exposed to total body irradiation but have specific endocrine issues, especially pubertal and growth delay related to iron toxicity. Experience is growing in HSCT in patients with haemoglobinopathies worldwide, but data on endocrine late-effects is scanty.

**Aims** To evaluate the endocrine late-effects seen in children with  $\beta$ -thalassaemia major( $\beta$ -thal) and sickle cell disease(SCD) post-HSCT focusing on gonadal, growth and thyroid effects.

**Methods** A retrospective audit was undertaken of all NHS patients aged less than 18 years who underwent HSCT and late-effects follow up at our centre from January 2001 to December 2011. The data was collected from hospital and electronic records.

**Results** 46 post-HSCT patients were identified; 29 with  $\beta$ -thal and 17 with SCD amounting to a total of 232 follow-up years. One patient(SCD) died on day 20 post-HSCT. Male to female ratio was 0.84(21/25). Median age at transplant was 8.68 years(range 2.2–17.6 years). 41/45(91.1%) patients received busulphan and cyclophosphamide as part of their conditioning regime. The remaining 4 received a reduced intensity regime(fludarabine, treosulfan, thiopate and thymoglobulin). These patients have been excluded from late-effect analysis.

Gonadotrophins were abnormally raised in 10/22(45.5%) females and 4/19(21.1%) males during post-HSCT follow-up. More females 9/16(56.3%) than males 1/10(10.0%) in the pubertal age group required either pubertal induction or sex steroid replacement. FSH(Mean 45.56U/L) was more elevated than LH(Mean 20.68U/L) in all 9 females, indicating ovarian damage. Estrogen was used for secondary amenorrhoea in 3 patients(all SCD).

Only 4/41(9.8%) patients had compensated hypothyroidism post-HSCT. None required treatment.

At least 2 points of growth data were available in 34/45 patients. SCD patients(mean height SDS-0.21) were taller than those with  $\beta$ -thal(mean height SDS-1.32) pre-HSCT. There was no significant change in height SDS during follow-up. Only 1 male( $\beta$ -thal) had severe growth failure with a low IGF-1 but a normal GH stimulation test. He responded well to empirical GH.

**Conclusion** Hormonal evidence of gonadal failure is more common post-HSCT in females than males. Growth and thyroid adverse effects are rare. Children with haemoglobinopathy seem to have a decreased burden of endocrine late-effects post-HSCT compared with oncology patients.

## G96 A NATIONAL SURVEY OF EVALUATION AND TREATMENT OF HYPERTENSION IN PAEDIATRIC PATIENTS WITH DIABETES

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**Aims** We conducted a postal survey of paediatric diabetic units in NHS Hospitals across the United Kingdom regarding their practise of evaluation and management of hypertension in paediatric patients with both Type 1 and Type 2 diabetes.

**Methods** A questionnaire was sent to different units across the UK. Addresses of units were identified from the directory of diabetic care 2008. Questionnaires were sent to 151 units in month of June 2012. Response was awaited for 12 weeks. 69 responses were received. The data were analysed using Microsoft excel.

**Results** Out of 151 units 69 units replied, giving a response rate of 45%. Of the units that replied, 10% of the units have written guidelines. 88% of the units have some form of age and height based chart to identify hypertension. 50% of the units check blood pressure annually during diabetic annual review whilst other more frequently. Only 45% of the units consider microalbuminuria as a trigger to initiate investigation. 73% of the units undertake 24 hours ambulatory blood pressure monitoring prior to starting antihypertensive therapy. For further confirmation and management of hypertension 62% of the units refer these children for joint management with nephrologist. Our survey revealed a wide variation and inconsistencies in practise of evaluation and management of hypertension in this high risk patient group. There is also a variation in the choice of antihypertensive medication amongst different units.

**Conclusion** There is a need for national consensus on evaluation and management of hypertension in children with diabetes which will help in standardisation of the care and consequently reduce the morbidity related to its long term complications.

## G97 RANGE OF URINARY STEROID METABOLITE RATIOS IN CHILDREN UNDERGOING INVESTIGATION FOR SUSPECTED DISORDERS OF STEROID SYNTHESIS

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**Background** Calculation of a urinary steroid metabolite ratio (uSMR) may be a useful method of improving diagnostic yield when investigating disorders of steroid hormone synthesis.

**Objective and hypothesis:** To investigate the range of uSMR in children with suspected disorders of steroid hormone synthesis.

**Population/Methods** Ten ratios were calculated on steroid metabolite data analysed by GC-MS in urine samples collected between 2008–2010 from 219 children who were undergoing investigations. To obtain reference data, urine samples were also analysed in 89 children with no background of endocrine concerns and who had a urine sample collected at presentation to the hospital with an acute illness.

**Results** Of the 89 reference children, 36(40%) were male and median age at time of the test was 3 yrs(range,1month-11yrs). Of

the 219 endocrine patients, 64(29%) were boys. In 129(59%) cases, a urine sample was collected to investigate early or exaggerated signs of adrenarche. Median age at test was 7.4yrs(1day-18yrs). Median and ranges of 2 steroid ratios used in the diagnosis of 21-hydroxylase deficiency are demonstrated in the Table.

Abbreviations: 17HP: 17-hydroxypregnanolone, PT: pregnanetriolone, THE: tetrahydrocortisone, THF: tetrahydrocortisol.

Abstract G97 Table 1

	<6months	6months – <10yrs	10yrs-18yrs
17HP/ (THE+THF+5alphaTHF)			
Reference boys	0.014(0.005–0.08)	0.005(0.00–0.25)	0.025(0.003–0.08)
Affected boys	0.014(0.005–0.102)	0.008(0.001–0.37)	0.017(0.001–0.183)
Reference girls	0.11(0.025–0.005)	0.006(0.00–0.033)	0.011(0.003–0.069)
Affected girls	0.026(0.006–0.089)	0.008(0.001–0.08)	0.02(0.003–0.089)
PT/(THE+THF+5alphaTHF)			
Reference boys	0.024(0.008–0.031)	0.021(0.00–0.283)	0.108(0.025–0.482)
Affected boys	0.046(0.003–0.186)	0.027(0.003–0.103)	0.049(0.019–0.693)
Reference girls	0.012(0.009–0.035)	0.019(0.006–0.128)	0.065(0.029–0.223)
Affected girls	0.039(0.013–0.187)	0.039(0.005–0.351)	0.085(0.044–0.299)

**Conclusions** These novel data show that reference ranges for urinary steroid metabolite data need to be age matched. Most children with suspected disorders of steroid synthesis have a ratio which is within the reference range and the identification of outliers will lead to better targeting of genetic analyses.

## G98 MULTIDISCIPLINARY ASSESSMENT FOR BARIATRIC SURGERY IN ADOLESCENTS: A PILOT PROJECT FROM A NATIONAL REFERRAL SERVICE

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**Introduction** Obesity has medical, social, psychological, familial and dietary underpinnings. We report the results of multidisciplinary assessments in adolescent bariatric surgery patients in the UK.

**Aim** 1. Multidisciplinary assessment of patients prior to bariatric surgery. 2. Compare outcomes from bariatric surgery to conventional treatment in the obesity clinic.

**Methods** 2F, 2M, mean age 14 yrs (12–18yrs) were selected for bariatric surgery. One boy with Oestrogenesis Imperfecta (OI) had decrease mobility secondary to excess weight. Mean BMI 45kg/m<sup>2</sup> (38–52 kg/m<sup>2</sup>). They were jointly assessed by a paediatrician and paediatric surgeon. Investigations completed: Full blood count, electrolytes, Vitamin D, liver ultrasound, fasting insulin and glucose. Secondary assessment by dietetics and child psychiatry looked at as binge patterns, night eating, comorbid psychopathology and family functioning. Quality of life score (Impact on weight on Quality-Kids IWQOL) and Becks Anxiety inventory (BAI) were performed. Operations were performed by a paediatric surgeon and experienced adult bariatric surgeon. Three had lap bands fitted, the boy with OI underwent a sleeve gastrectomy. Pre and post surgery data were collected.

**Results** All surgical patients lost weight over 3 months. Mean loss –10kg/m<sup>2</sup> (5–17 kg/m<sup>2</sup>). The non surgical group had a mean gain +1.9kg/m<sup>2</sup> (–4 – 10 kg/m<sup>2</sup>). Improvement in clinical parameters was also seen: insulin resistance (HOMA-IR) fell from 4.5 to 1.7, mean systolic blood pressure (mmHg) dropped 139 to 126, mean waist circumference (cm) from 121 to 116 cm, hepatic steatosis disappeared in 3 patients who demonstrated it and Vitamin D (µg/l) levels rose from 10 to 35.4. There were no significant complications. Constipation and nausea reported in 2 of the 4. All patients reported improvement in their well being. IWQOL improved mean scores in