128,531 newborns. We detected 48 patients with IMDs. Disturbed metabolism of vitamins was detected in 9 patients with partial biotinidase deficiency (prevalence (P) 1:14,500) and in 3 patients with maternal vitamin B12 deficiency (P 1:44,000). We did not detect any newborn with riboflavin or coenzyme Q deficiency. The treatment with biotin or vitamin B12 prevented development of clinical symptoms in all patients. Addition of biotinidase activity and of low methionine with second-tier total homocysteine measurement led to increase of the detection rate from 1:3600 to 1:2700 and enabled an early and an efficient treatment of affected patients.

P25. Carnitine Deficiency in Preterm Neonates Receiving Total Parenteral Nutrition: Experience from Newborn Screening in Qatar

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Carnitine is an amino acid which plays an important role in the oxidation of long-chain fatty acids. Both infant formulas and breast milk contain carnitine. However, it is not routinely provided in parenteral nutrition solutions in Qatar. Preterm neonates have a reduced capacity to synthesize carnitine and may need supplementation if on long-term total parenteral nutrition (TPN). Newborn screening (NBS) in Qatar is performed on dried blood spots (DBS) collected at or after 36 h of birth. For preterm infants born before 32 weeks gestational age (GA), a successive DBS is collected at 32 weeks GA equivalent. This helps to identify metabolic disorders that may be missed on the initial card due to prematurity, and to diagnose carnitine deficiency related to TPN. The amino acid/acylcarnitine (AA/AC) profile on the DBS was obtained by tandem mass spectrometry analysis of the butyl esters. We collected data for the premature babies with AA/AC profile showing carnitine deficiency (low C0 acylcarnitine) on the initial and/or successive 32-week GA equivalent DBS, for the years 2016 and 2017. A total of 8.36% premature babies were diagnosed with carnitine deficiency related to TPN during this period. Of these 3.04% of the babies were diagnosed on the initial NBS and 5.32% on the successive 32-week NBS with first screen being normal. Neonates who were diagnosed with carnitine deficiency on the first DBS had gestational age at birth ranging between 23 weeks and 29 weeks, and birth weight between 620 g and 1090 g. Most of these babies had at least three low markers on the AA/AC profile (low C0, C2, C3, C16, C18, C18:1, Acs/Cit). These babies were supplemented with L-carnitine. Currently there is no evidence in the literature to support the routine supplementation of all parenterally fed premature babies with L-carnitine. Our practice of performing the NBS again at 32 weeks GA equivalent in extremely premature babies, helps to identify the ones which have carnitine deficiency secondary to TPN and supplement them with L-carnitine for optimal growth.

P26. Molecular Screening of IN2G (c.293-13A/C > G) Mutation and Detected Genotypes among the Macedonian Patients with Classical form of 21-Hydroxylase Deficiency

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Steroid 21-hydroxylase deficiency is present in 90–95% of all cases with congenital adrenal hyperplasia, an autosomal recessive disorder. Severe enzyme deficiency can present as a classical salt-wasting (SW) and simple virilizing form (SV). The In2G (c.293-13A/C > G) mutation in CYP21A2 gene, coding for 21-hydroxylase, abolishes enzyme activity on 0–1% of normal activity. It alters pre-mRNA splicing by activating another acceptor site for the splicing process and thus shifting the reading frame to create premature termination of translation. Fifty-seven DNA samples from Macedonian patients with clinical and laboratory signs of classical form of 21-hydroxylase deficiency,

25 SW and 32 SV, were collected and subjected to PCR/ACRS method for the detection of seven CYP21A2 point mutations (P30L, In2G, Del 8ntG110, I172N, V281L, Q318X and R356W). The patients were evaluated at the Department of Endocrinology and Genetics, University Pediatric Clinic, Skopje, Macedonia. Aberrant splicing mutation In2G (c.293-13A/C > G) was detected in 72% (18/25) of the SW patients on 66% (33/50) alleles, and in 40.6% (13/32) of the SV patients on 31.25% (20/64) of the alleles. The most prevalent was In2G/In2G genotype found in 15 (60%) SW and 7 (21.9%) SV patients. The other genotypes detected among SW patients were In2G/Q318X in 2 and In2G/V281L + Q318X + R356W in 1 patient. Among the SV patients were detected In2G/P30L genotype in 3, In2G/I172N in 1 patient, and two were heterozygotes for In2G with no detected mutation on the second allele. The In2G/In2G was the most prevalent genotype among the Macedonian patients with classical 21-hydroxylase deficiency. Our founding supports the role of the In2G mutation in classical phenotype of the disease.

Keywords: 21-hydroxylase deficiency; CYP21A2 gene; In2G mutation; genotype

P27. Effect of Clinical and Environmental Factors on 17 Hydroxy Progesterone and Its Cut-off Values in Newborns-Insights from a Prospective Newborn Screening Project in Delhi State

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To evaluate correlation between 17-OHP values and various clinical and environmental parameters, and to establish cut-off values for 17-OHP such that optimum sensitivity and lower recall is maintained in the Newborn screening program for congenital adrenal hyperplasia. Multicentric program including 20 state funded hospitals in the state of New Delhi, India from Nov 2014 to March 2017. Heel prick sample of 202,549 newborns were taken as a part of multicenter Newborn screening program. 17-OHP levels were determined on a Genomic Screening Processor by fluoroimmunoassay. Log transformation of 17-OHP values was done to test for effect of various variables (such as gestational age, birth weight, gender, age at sampling, type of feeding, season of birth) on 17-OHP values using linear regression and multivariable regression analysis. Three set of cut-off values, based on 17-OHP values in true positive cases and 99th percentile values of data were determined. Cut-off 1 was an absolute value 50 ng/mL for preterm and low birth weight infants and 37.5 ng/mL for full term infants. Cut-off 2 and 3 were based on gestational age and birthweight intervals. Recall rate, false positive rate and ROC curve were calculated for each set to test for accuracy of each. Gestational age, birth weight and postnatal age at sampling were significant negative predictors of 17-OHP values. All three cut-off values had reduced recall rates with cut-off 1 having the lowest. Area under ROC curve was maximum for gestational age-based interval cut-off. Cut-off with lower recall rates which will not compromise on overall accuracy should be preferred and used.

P28. Wisconsin Screening Algorithm for Congenital Adrenal Hyperplasia: Addition of a Second-Tier Steroid Profile Assay

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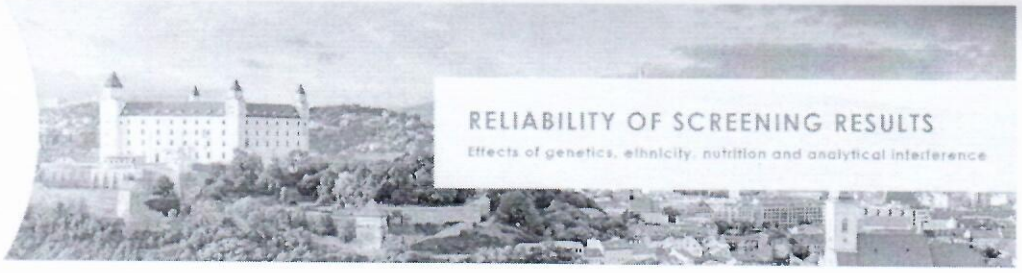
Newborn screening for congenital adrenal hyperplasia (CAH) has one of the highest false positive rates of any of the diseases on the Wisconsin panel. This is largely due to the first-tier immune assay cross reactivity and physiological induced changes in concentration of 17-hydroxprogesterone during the first few days of life To improve screening for CAH, Wisconsin developed a second-tier assay to quantify five different steroids (17-hydroxyprogesterone, 11-deoxycortisol, 21-deoxycortisol, androstenedione, and cortisol) by liquid chromatography tandem mass spectrometry (LC-MSMS) in dried blood spots, using previously published papers as reference. The method validation included



CERTIFICATE OF ATTENDANCE

We herewith certify that

Violeta Anastasovska
Macedonia, The Former Yugoslav Republic Of

has attended the

ISNS 2018
11th ISNS European Regional Meeting
in Bratislava
from the 14th to the 17th October 2018

Dr Maria Knapkova
LOC Chair

Dr Rodney Howell
ISNS President