Background FHHNC is a rare autosomal recessive tubulopathy of the thick ascending limb due to inactivating mutations in the Claudin-té and Claudin-t nine genes which are responsible for the paracellular reabsorption of calcium and magnesium. Clinically, FHHNC is characterized by urinary tract infections, nephrolithiasis, nephrocalcinosis and progressive renal failure.

Objective To present clinical and molecular data on 2 siblings with FHHNC and early onset SND, found to have a new mutation in the Claudin-té gene.

Methods A 16-year-old male and his 14-year-old sister were diagnosed with chronic kidney disease since early infancy, manifested by recurrent UTIs, polyuria and polydipsia, poor growth, mild mental retardation and delayed speech. SND was diagnosed at the age of 6 and 7 years. Both have hypomagnesemia, hypermagnesuria, hypercalciuria and nephrocalcinosis. Genotyping was performed by PCR using tetranucleotide repeat polymorphisms. Specific primer pairs of genomic DNA were used as template for sequencing the Cldn16 gene.

Results Exons 1, 2, 4 and 5 were amplified and revealed wild type sequencing but exon 3 failed in amplification by PCR. Long range PCR spanning exon 2 to 4 of the gene yielded a 2.5 kb fragment shared by the patients. Sequencing of this fragment reveal a 2630 bp deletion including the entire exon 3 resulting in deletion and frame shift of Cldn16 protein.

Conclusion This family demonstrates the first identified homozygous mutation in the Cldn-té gene causing the deletion of an entire exon. This, however, is unlikely to explain the SND, since this gene is not expressed in the cochlea.

Abstract 1203 Figure 1

Conclusions ODM have higher SBP than controls. This increase is independent of type of maternal diabetes and may be related to maternal pre-pregnancy BMI. Gender-specific differences require further investigation.

Abstract 1203

Background and Aims Offspring of diabetic mothers (ODM) are at increased risk of the metabolic syndrome in later life. We aimed to perform a systematic review and meta-analysis of studies examining offspring systolic and diastolic blood pressure (SBP, DBP) in childhood in relation to maternal diabetes.

Methods Citations were identified in PubMed. Authors were contacted for additional data where necessary. SBP and DBP in ODM and controls were compared. Subgroup analysis was performed according to type of maternal diabetes and offspring gender. A fixed effect meta-analysis was performed, and a random effects analysis where significant heterogeneity was present. Meta-regression was used to test the relationship between offspring SBP and maternal pre-pregnancy BMI.

Results Fifteen studies were included in the systematic review and thirteen in the meta-analysis. SBP was 1.88mmHg higher in ODM (95% CI 0.47, 3.28; p=0.009). The increase in SBP was similar in both offspring of mothers with gestational diabetes (1.39mmHg [0.00, 2.77]; p=0.05) and type 1 diabetes (1.64mmHg [0.09, 3.18]; p=0.04). Male ODM had higher SBP (2.01mmHg [0.93, 3.10]; p=0.0003) and DBP (1.12mmHg [0.36, 1.88]; p=0.004) than controls, but the differences in SBP and DBP between female ODM and controls were not statistically significant. Offspring SBP was positively correlated with maternal pre-pregnancy BMI; however, the association was not significant (p=0.37).