SUPPLEMENTARY DATA

Supplementary Materials

High Sensitivity CRP analysis was undertaken on a routine analyser in the Biochemistry department at the Royal Devon and Exeter NHS Foundation Trust, Exeter, UK using the Roche Diagnostics (Mannheim, Germany) P800 modular system. The assay is a Particle enhanced immuno-turbidimetric method. Human CRP agglutinates with latex particles coated with monoclonal anti-CRP antibodies. The precipitate is determined turbidimetrically at 552nm. The method has an intra assay CV of <1.5%, inter assay CV of <2.1 % and a lower detection limit of 0.15 mg/L. This method has been standardized against the CRP reference preparation of the Institute for Reference Materials and Measurements (IRMM) BCR470/CRM470 (RPPHS - Reference Preparation for Proteins in Human Serum)

Study Participants

The 540 MODY patients (from 359 different families) with a confirmed molecular genetic diagnosis patients were recruited through the molecular genetic diagnostic service at the Royal Devon and Exeter NHS Foundation Trust which provides an international service for molecular genetic testing of monogenic diabetes. The 53 patients with a clinical diagnosis of Type 1 diabetes (defined as age of diagnosis <30 years and on insulin since diagnosis) and 157 patients with a clinical diagnosis of Type 2 diabetes (defined as age of diagnosis $\geq$35 years and not on insulin for the first year of diagnosis) were recruited from Exeter based clinics. All samples were stored at -80^{o}C prior to analysis.

Statistical analysis

Results are presented as median (inter-quartile range) unless otherwise stated. High sensitivity CRP showed a skewed distribution and so was log transformed and data presented as geometric means and back transformed standard deviation (SD) range and confidence intervals (CI). General linear models were used to investigate the impact of covariates (age of diagnosis, BMI, HbA1c, current age) on hsCRP levels, Residuals were checked to ensure model assumptions were met.

Receiver Operating Characteristic (ROC) Curves were used to assess the discrimination of HNF1A-MODY from other subtypes of diabetes and to identify cut-offs of hsCRP that achieve the optimal sensitivity and specificity. Statistical analysis was performed in SPSS version 17 (PASW) and Mann-Whitney U was used to compare medians, $p<0.05$ was assumed significant.

Supplementary Results

Analysis of potential confounders

Regression analysis was used to determine the impact of covariates (age of diagnosis, BMI, HbA1c, current age) and determine whether they were confounders on the discriminatory power of hsCRP to identify HNF1A-MODY from other diabetes subtypes. Using a step wise approach BMI and age of diagnosis were found to be the only independent predictors of hsCRP (beta (CI)= 0.079 (0.057-0.1), p=<0.001 and 0.014 (0.05-0.023), p= 0.002 respectively. After adjustment for these two variables hsCRP was still significantly lower in the HNF1A-MODY group (see supplementary table 1).

SUPPLEMENTARY DATA

Supplementary Table 1. Clinical characteristics of each diabetic subgroup

	Type 1 diabetes n=53	**Type 2 diabetes n=157**	**HNF1A-MODY n=220**	**HNF4A-MODY n=54**	**HNF1B-MODY n=21**	**GCK-MODY n= 245**
%Male	47.5	56.2	41.1	26.8	47.6	35
Age of diagnosis	21.3 (17.9-24.7)	61.6 (59.6-63.6)	21.5 (20.25-22.8)	23.5 (19.7-27.3)	20.5 (11.74-29.3)	25.2 (23.1-27.3)
Duration	21.9 (16.7-27.2)	9.2 (8.03-10.35)	17.5 (15.6-19.3)	13.7 (10.2-17.2)	8.8 (3.4-14.2)	8.4 (6.9-9.9)
BMI	24.8 (23.7-25.8)	28.6 (27.7-29.4)	24.9 9 (24.1-25.8)	24.2 (22.2-26.3)	23.6 (19.6-27.6)	23.0 (22.3-23.8)
HbA1c	8.0 (7.6-8.4)	7.9 (7.6-8.3)	7.6 (7.3-7.9)	8.1 (7.4-8.8)	8.6 (7.2-10.0)	6.5 (6.4-6.6)
hsCRP (mg/L) (Geometric Mean (SD range))	1.02 (0.36-2.88)	1.71 (0.52-5.57)	0.34 (0.11-1.05)	1.43 (0.38-5.42)	0.75 (0.17-3.35)	0.79 (0.19-3.31)
Adjusted hsCRP (mg/L) (Geometric mean (CI))*	1.34 (1.19-1.91)	0.90 (0.67-1.25)	0.42 (0.33-0.53)	1.98 (1.31-3.00)	1.26 (0.58-2.74)	1.09 (0.87-1.37)
P value vs HNF1A-MODY **	<0.001	0.012	NA	<0.001	0.11	<0.001
hsCRP (mg/L) (Median (IQR))	1.10 (0.50-1.85)	1.4 0(0.60-3.45)	0.30 (0.10-0.60)	1.45 (0.45-2.88)	0.60 (0.1-2.85)	0.60 (0.30-1.80)
P value vs HNF1A-MODY ***	<0.001	<0.001	NA	<0.001	0.07	<0.001

* Adjusted for BMI and age at diagnosis, **p value calculated using Bonferroni adjusted pairwise comparisons in ANOVA , ***p value calculated by Kruskall-Wallis NA = not applicable. Data presented as median (IQR) unless otherwise stated.

SUPPLEMENTARY DATA

Supplementary Figure 1. Box plot and Receiver Operating Characteristic (ROC) curve to identify HNF1A MODY from Type 2 diabetes. Supplementary Figure 1A. Boxplot to show serum hsCRP in HNF1A (n=220) and Type 2 diabetes (n=157). Dotted line indicates an hsCRP cut off of 0.75 mg/L. Box= Median and IQR, whiskers= data range, Dots= outliers (>1.5x IQR), Stars=extreme values (>3x IQR). Excluding all subjects with hsCRP levels >10 mg/L. **Supplementary Figure 1B.** The ROC Curve identified a cut-off hsCRP <0.75 mg/L for discriminating HNF1A MODY from Type 2 diabetes (area under curve 0.84) with 79% sensitivity and 70% specificity