

Determination of pancreatic hormones in children with different forms of hyperinsulinaemic hypoglycaemia

BACKGROUND In congenital hyperinsulinism (CHI) hypoglycaemia results from a dysregulation of insulin secretion. We hypothesised that other pancreatic hormones may also be dysregulated in this condition.

OBJECTIVE To proof the applicability of Luminex Multiplex method to measure pancreatic hormones (insulin, C-peptide, glucagon, amylin and pancreatic polypeptide (PP)) in the paediatric age. To elucidate the fasting response of these hormones in children with different forms of CHI.

SUBJECTS AND METHODS 12 children (seven females) with ages between 11 days of life and 13 years had the plasma pancreatic hormones extracted at normoglycaemia and at hypoglycaemia (end of fast). The patients have different CHI aetiologies, histology types and different response to treatments. The hormones were analysed using multiplexing manner on 0.025 ml of plasma.

RESULTS

Patients' characteristics:

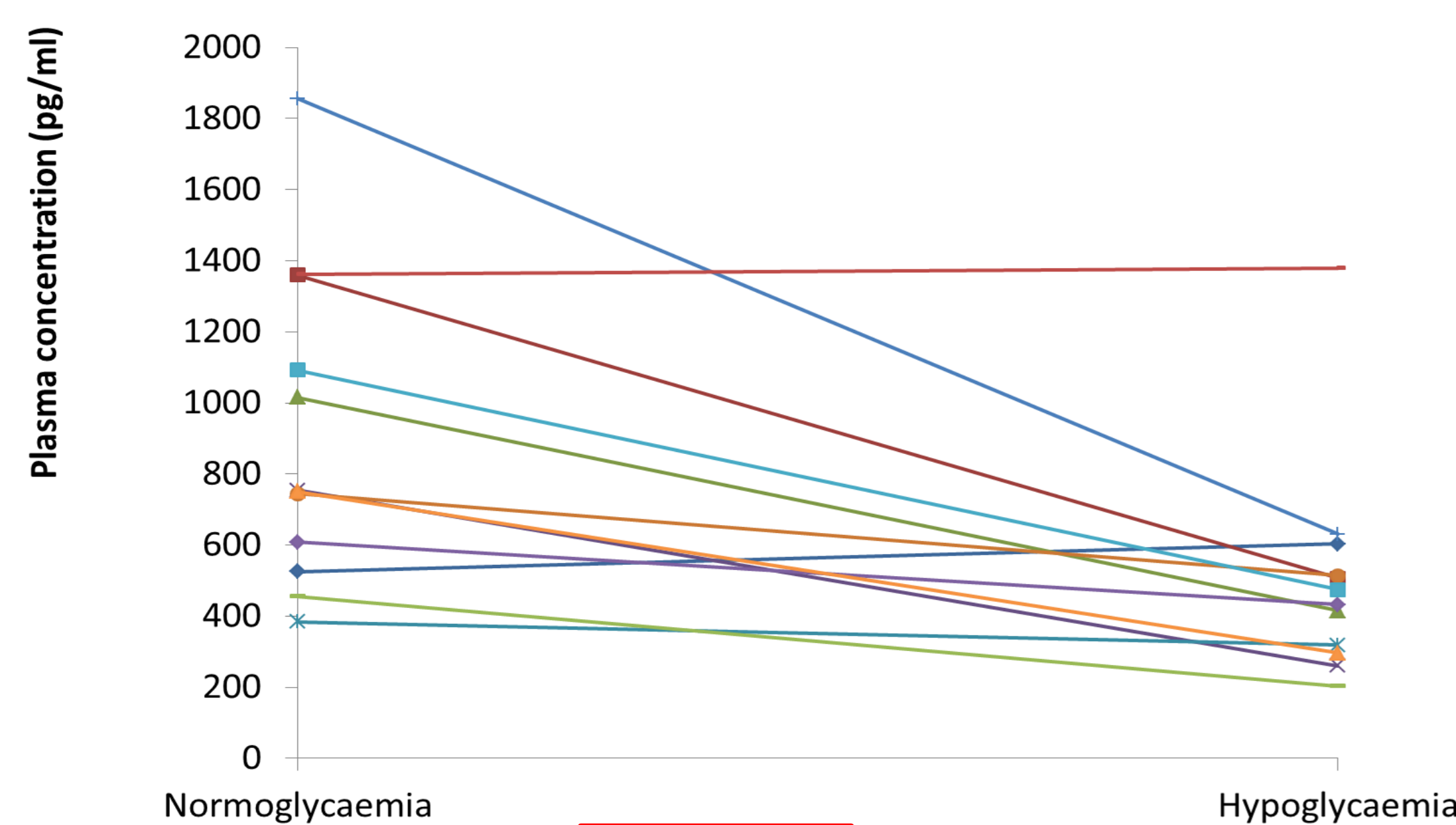
Patient ID	Gender	Age	Feeding Route	CHI treatment	Medications	Responsive to this Treatment	Pancreatectomy	Genetics for CHI	Histology/PET scan
1	Male	1y6m	Oral	20% Dex	No	No	No	Negative	Diffuse
2	Male	14d	Oral	25% Dex	No	No	No	Maternal heterozygous <i>ABCC8</i>	Diffuse
3	Female	3m	Oral	20% Dex	Octreotide, Domperidone, Lansoprazole	Yes	Lesionectomy	Paternal heterozygous <i>ABCC8</i>	Focal
4	Male	4y1m	Oral	10% Dex	Tompsonate, Levetiracetam, Clonazepam, Azithromycin	No	Lesionectomy	Negative	Focal
5	Female	9m	Oral	15% Dex	No	No	Lesionectomy	Paternal <i>KCNJ11</i> non stop mutation	Focal
6	Male	11d	Oral	Dex	No	Yes	No	Negative	?
7	Female	2m	Continuous	40% Dex	Glucagon	No	No	Negative	Diffuse
8	Female	1m7d	Oral	30% Dex	No	No	No	Negative	Diffuse
9	Male	5m	Oral	20% Dex	No	No	Subtotal	Homozygous <i>ABCC8</i>	Diffuse
10	Female	9m	NG	Dex	No	No	No	Negative	?
11	Female	2m	Oral	Dex	No	No	No	Negative	?
12	Female	13y	Oral	No	No	Not applicable	No	Negative	?

PET: 18F-dopa-Positron Emission Tomography Scan; y: years; d: days; m: months; Dex: Dextrose

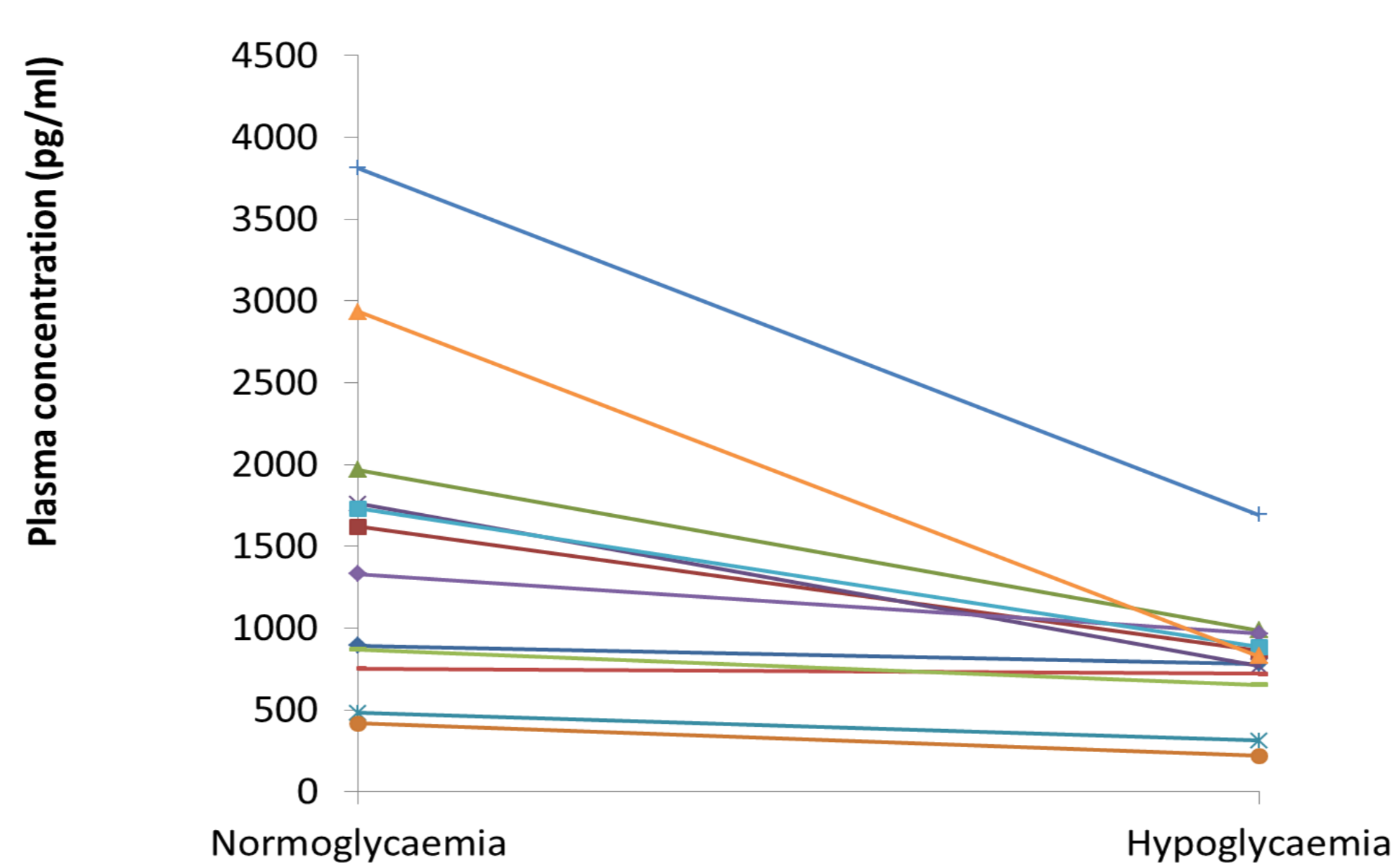
Hormone analysis:

	NORMOGLYCAEMIA				
	Amylin Total	C-Peptide	Glucagon	Insulin	PP
Average	34.6	1546.8	97.3	909.2	83.8
SEM	7.3	292.5	72.0	127.5	30.7
SD	21.8	1013.1	238.8	441.5	106.5
Mean +2SD	78.3	3573.0	574.9	1792.2	296.7
Mean -2SD	-9.1	-479.4	-380.2	26.2	-129.1
t test CHI N vs. H	0.014	0.005	0.214	0.004	0.654
n	9	12	11	12	12
	HYPOGLYCAEMIA				
	Amylin Total	C-Peptide	Glucagon	Insulin	PP
Average	21.2	805.5	103.3	502.8	85.7
SEM	3.5	105.5	75.1	88.5	33.1
SD	9.3	365.6	260.0	306.4	114.6
Mean +2SD	39.8	1536.8	623.3	1115.7	314.9
Mean -2SD	2.5	74.3	-416.7	-110.1	-143.5
n	7	12	12	12	12

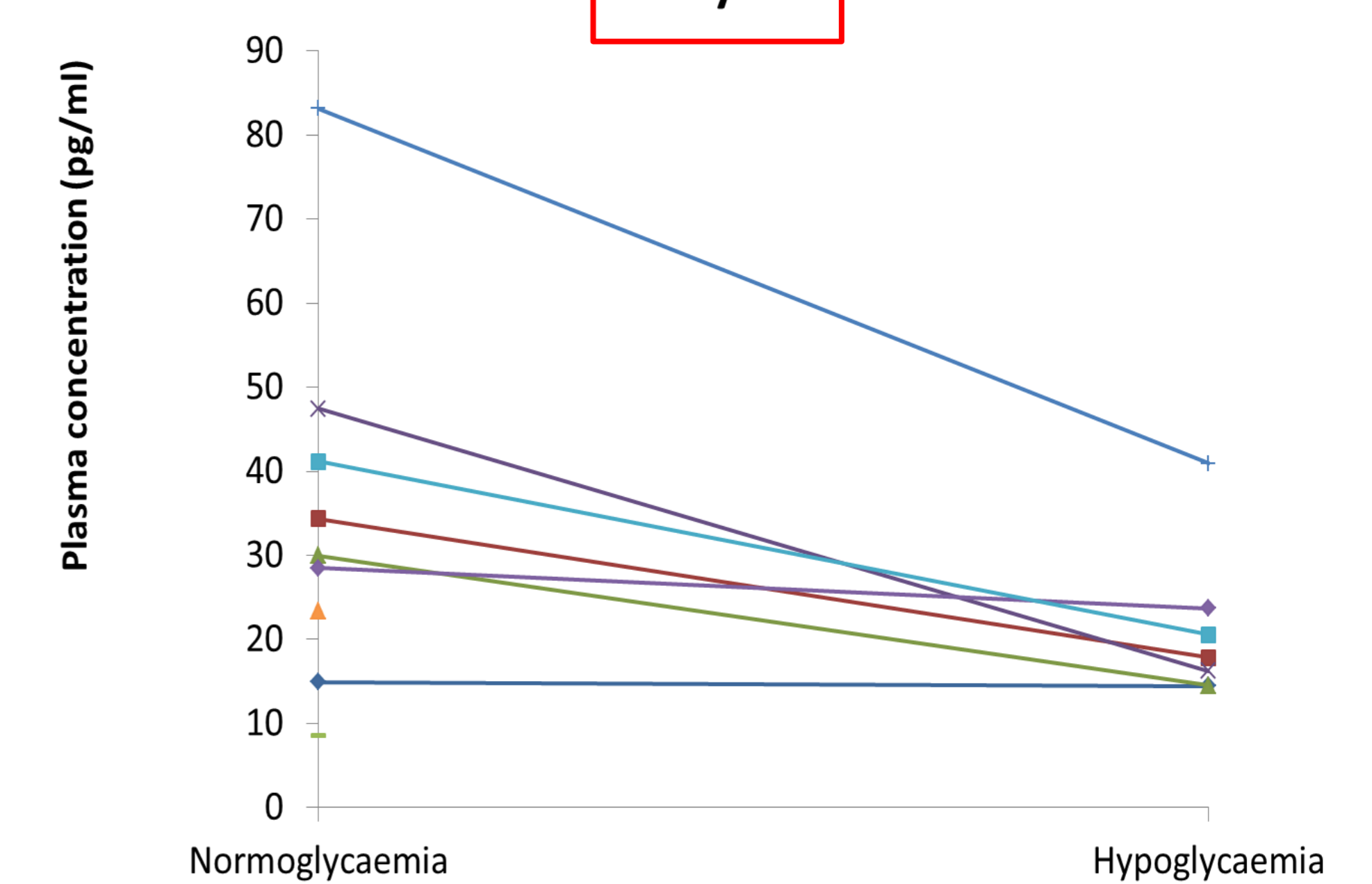
Insulin



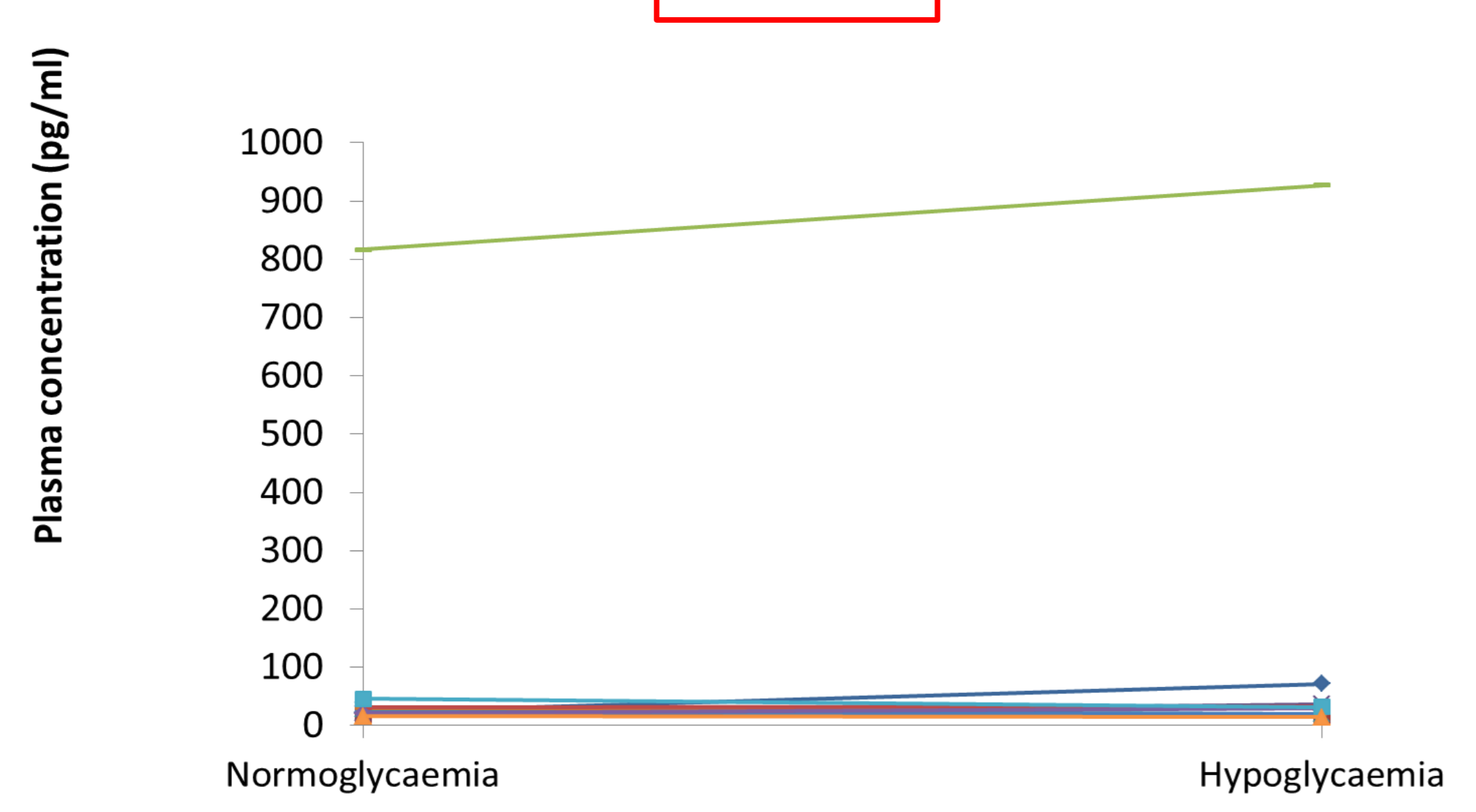
C-Peptide



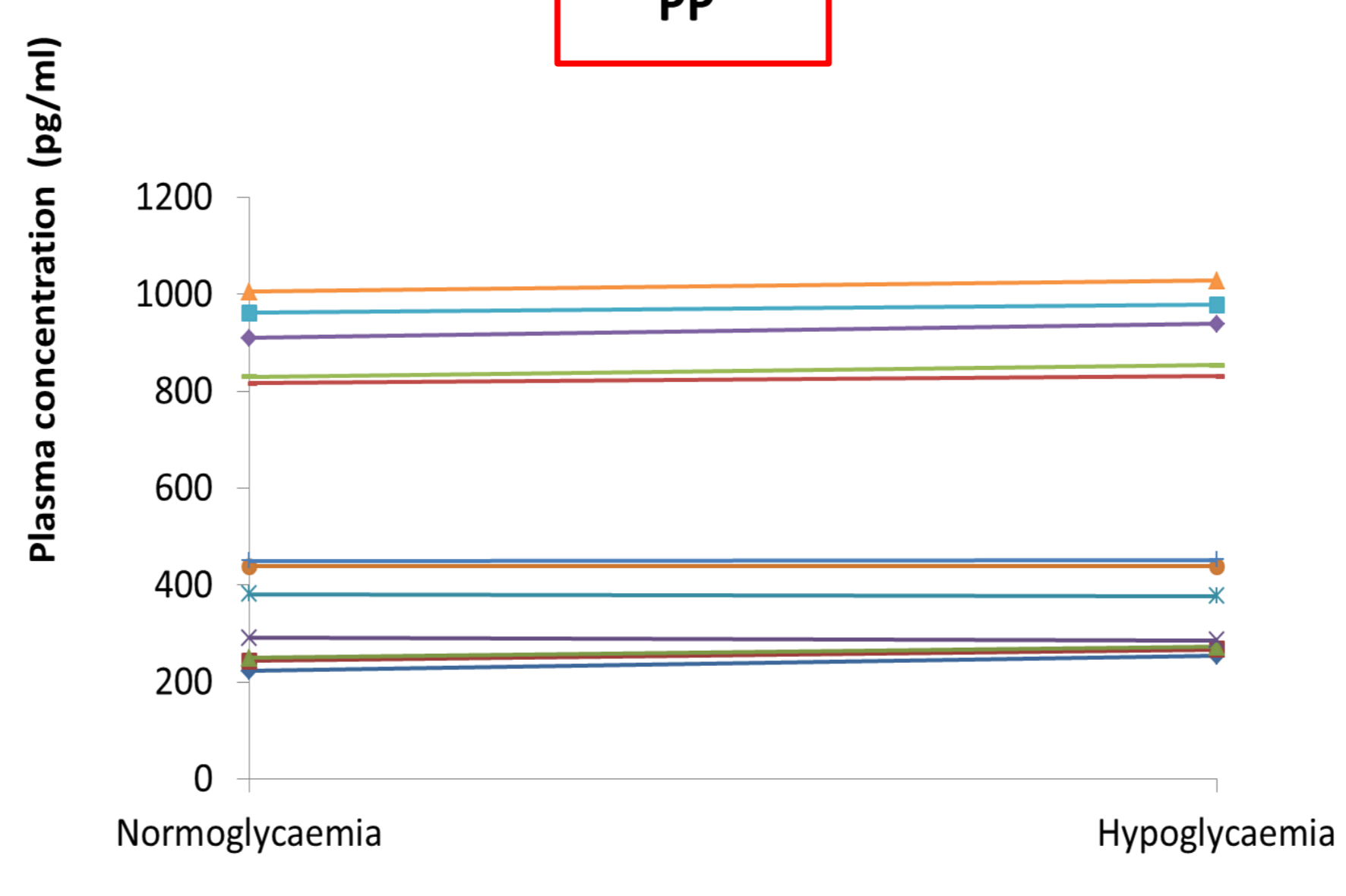
Amylin



Glucagon



PP



CONCLUSIONS

- This assay demonstrates its suitability to determine pancreatic hormones in the paediatric age group.
- In children with CHI, glucagon's response to hypoglycaemia is impaired.
- No previous reports have determined amylin concentrations in CHI, and this study indicates that it decreases during hypoglycaemia to avoid its anorectic effect, although interestingly PP's concentrations remain stable despite hypoglycaemia.

REFERENCES

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-Papastamataki M et al. Incretins, amylin and other gut-brain axis hormones in children with coeliac disease. *Eur J Clin Invest*. 2014 Jan;44(1):74-82
-Hussain K et al. Serum glucagon counterregulatory hormonal response to hypoglycemia is blunted in congenital hyperinsulinism. *Diabetes* 2005;54:2946-2951