

# Investigating the role of pancreatic hormones in Congenital Hyperinsulinism

## INTRODUCTION

Congenital hyperinsulinism (CHI) is a cause of persistent hypoglycaemia. Children with CHI have dysregulated insulin secretion and very often present feeding issues. Amylin and pancreatic polypeptide (PP) are produced in the pancreas and have been reported to have anorectic action on feeding and therefore it is possible that they could also be dysregulated in CHI. We investigated the response of pancreatic hormones (insulin, C-peptide, amylin and PP) after a fast in children diagnosed with CHI due to different underlying mechanisms.

## MATERIALS AND METHODS

Plasma pancreatic hormones were collected in 12 children with CHI at GOSH. Once consent was obtained from parents, the samples were collected at normoglycaemia and at hypoglycaemia (end of fast). Analysis of the hormones was performed in multiplexing manner (Luminex Multiplex assay) on 0.025ml of plasma<sup>1,2</sup>. The multiplex plate containing the beads, antibodies and plasma is run on a Luminex machine where the median fluorescent intensity data is analysed using a weighed 5-parameter logistic or spline-fitting method for calculating analyte concentrations.

## RESULTS

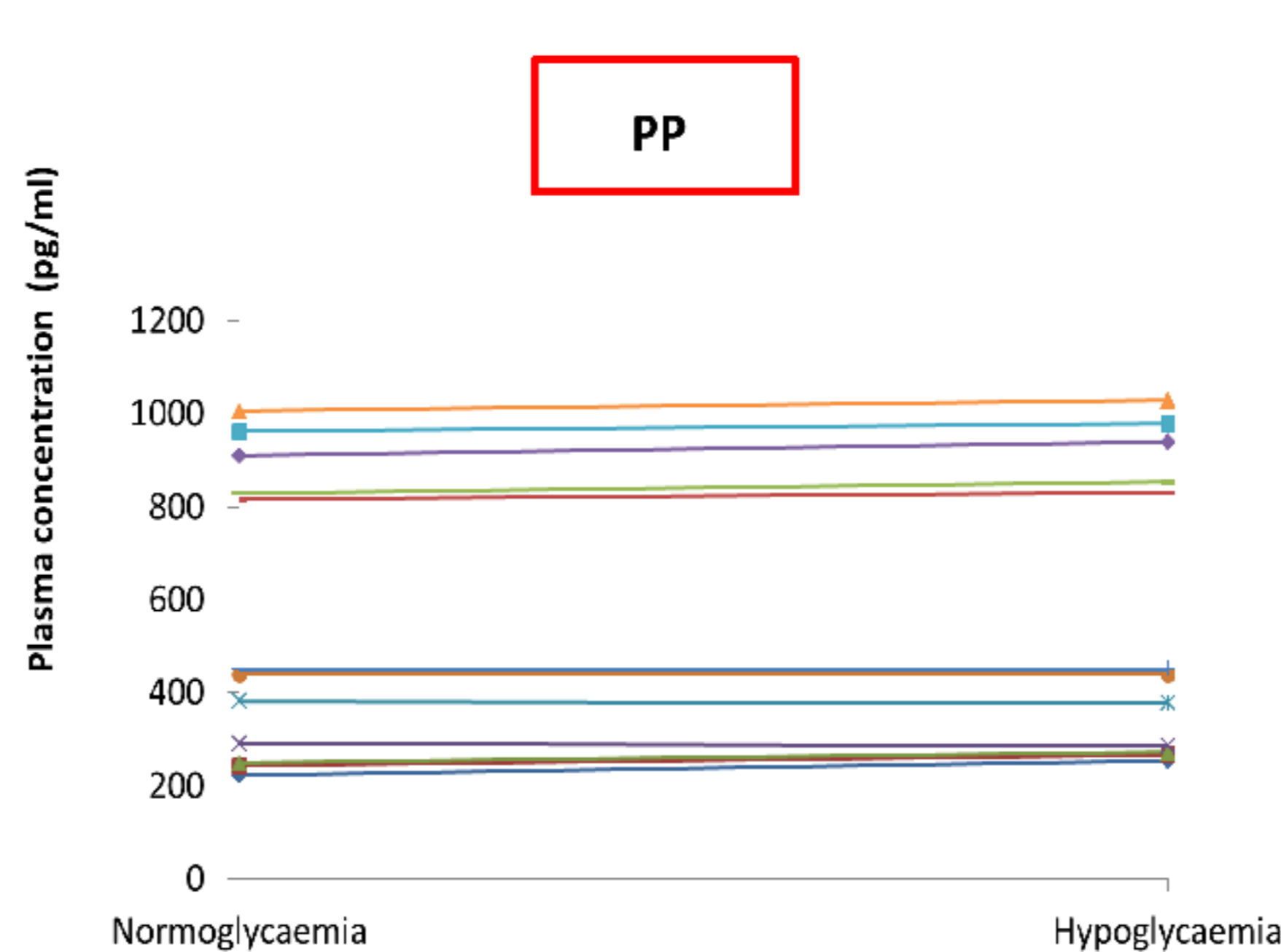
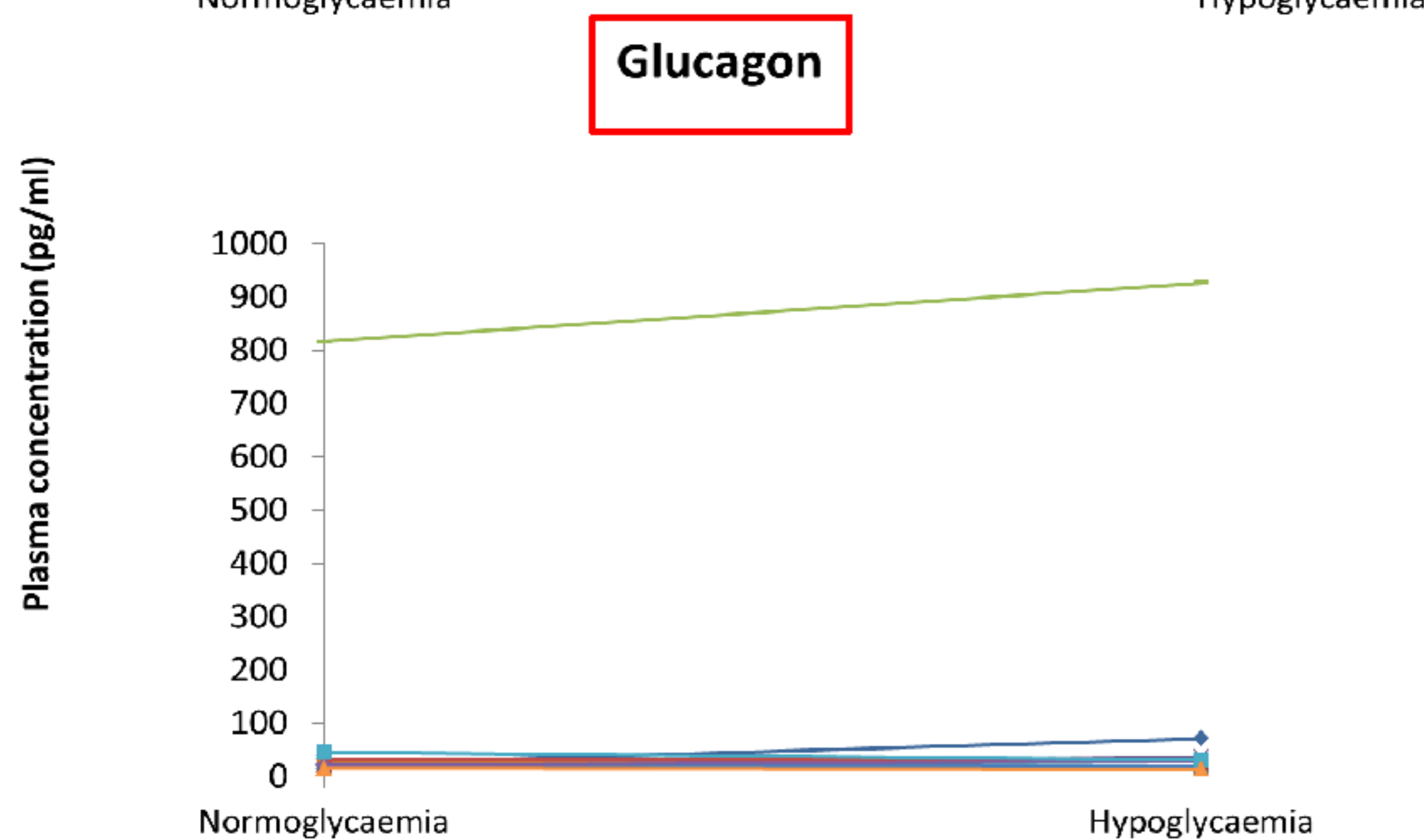
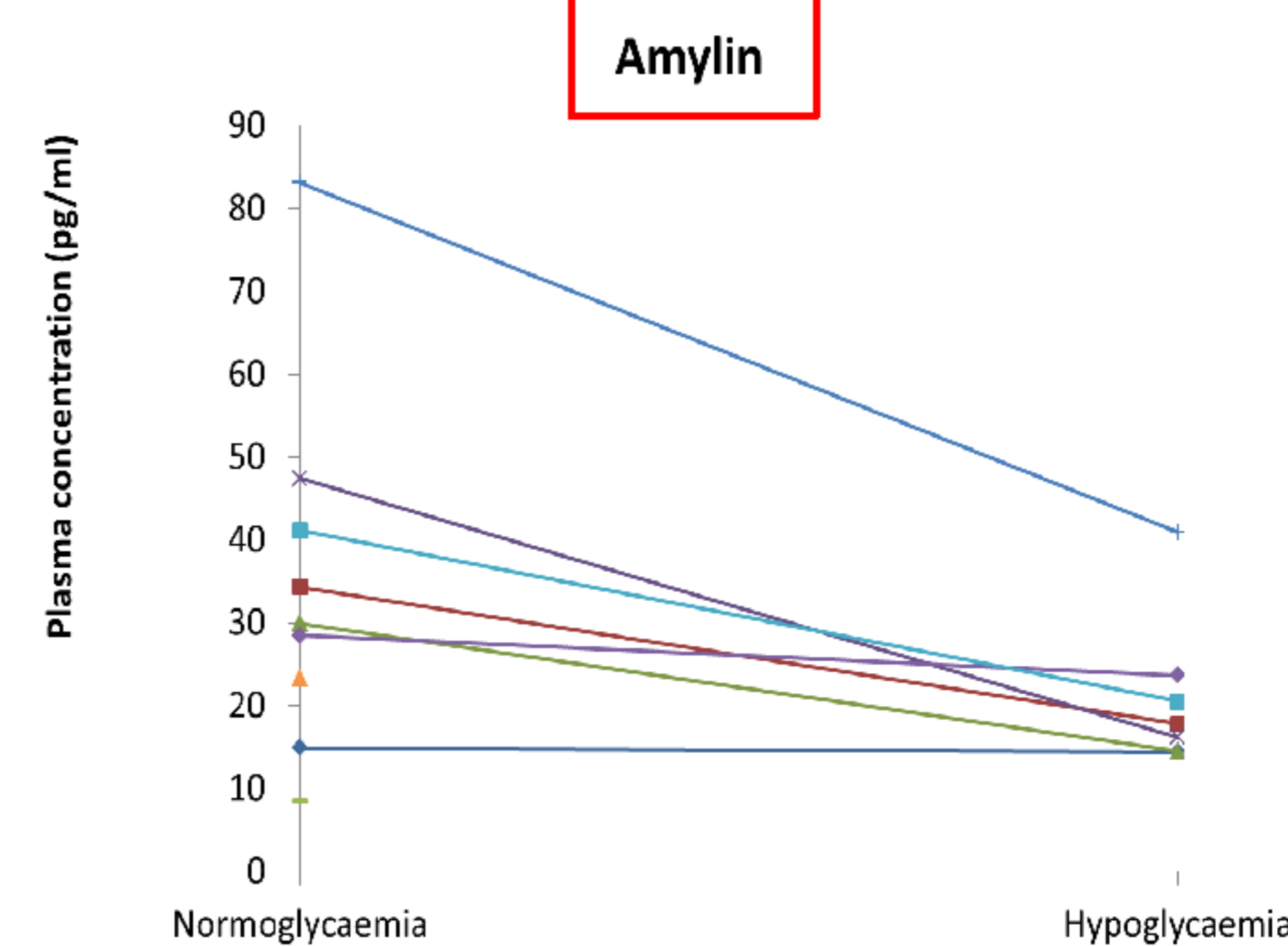
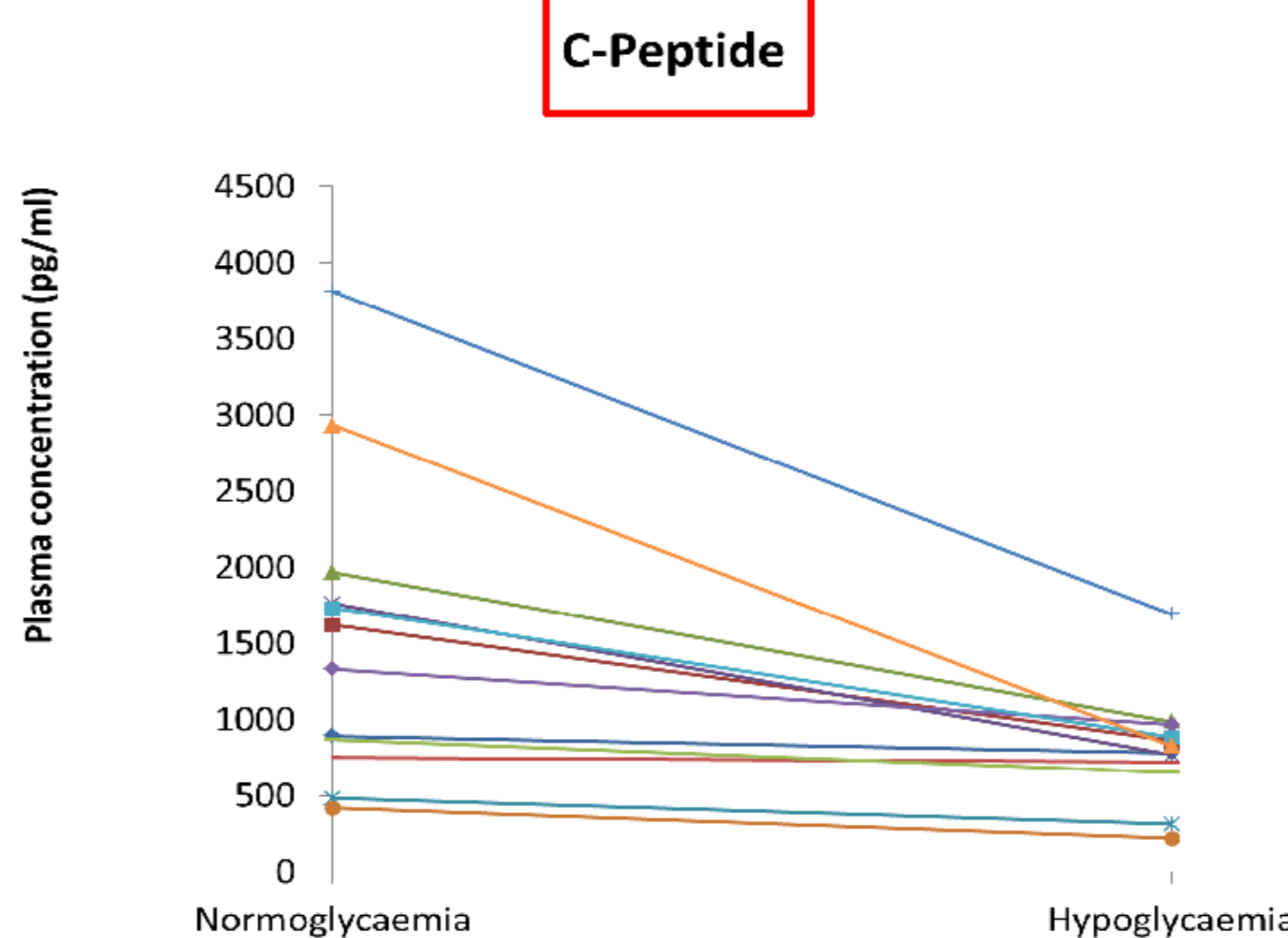
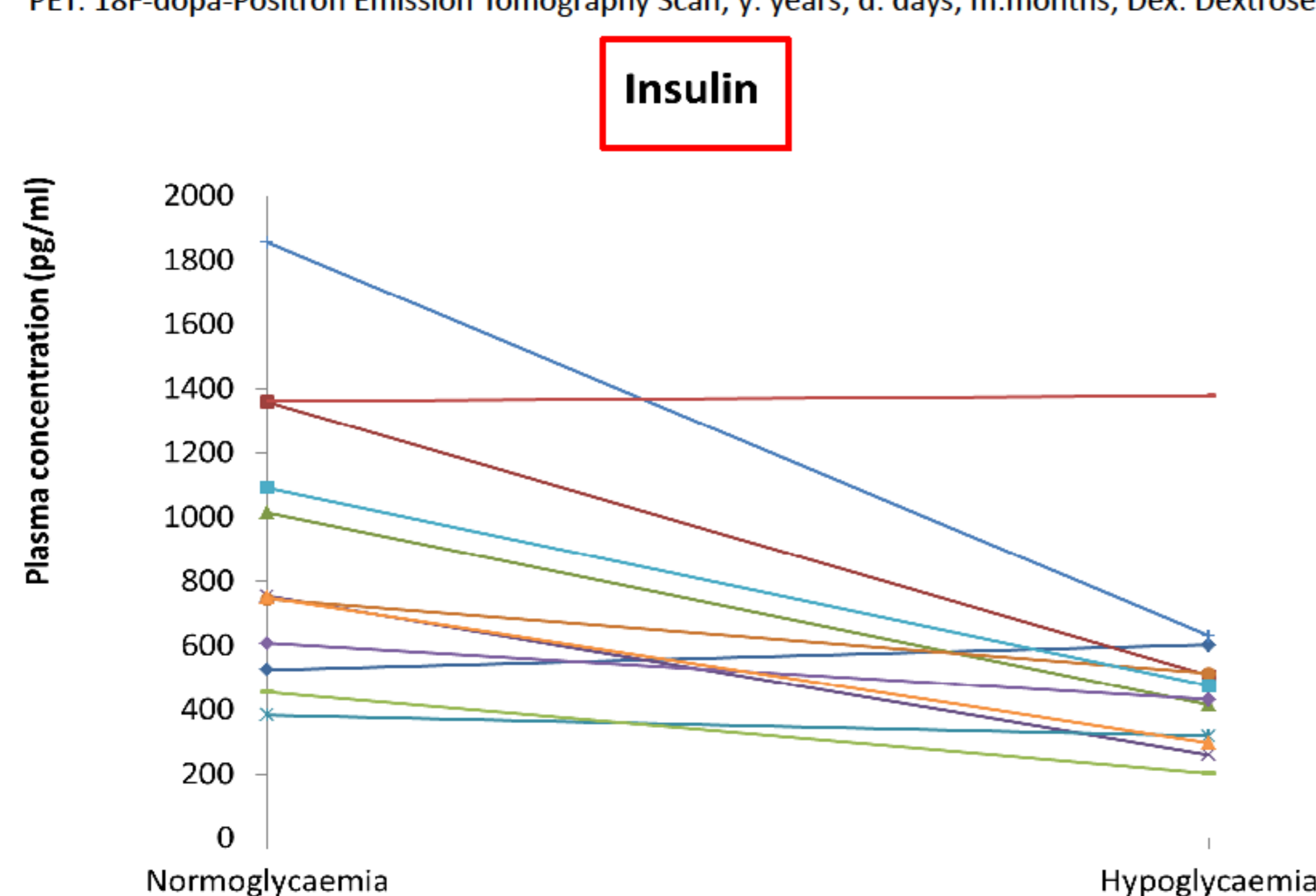
### Patients' characteristics:

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	Topiramate, 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	CHI/ ?Insulinoma

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	<b>0.014</b>	<b>0.005</b>	<b>0.214</b>	<b>0.004</b>	<b>0.654</b>
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



## CONCLUSIONS

- This assay has now proven to be useful in determining pancreatic hormones in children
- This study confirms that glucagon's response to hypoglycaemia is impaired in children with CHI<sup>3</sup>
- This is the first study to look at amylin concentrations in CHI
- Amylin decreases during hypoglycaemia so as to avoid its anorectic effect, but interestingly PP's concentrations remain stable despite hypoglycaemia, possibly indicating a paracrine effect that needs to be confirmed at the pancreatic level

## REFERENCES

- 1.- Hum M et al. Gut peptide hormones and pediatric type 1 diabetes mellitus. *Physiol Res.* 2011;60(4):647-58. Epub 2011 May 16.
- 2.- Papastamatakis 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
- 3.- Hussain K et al.. Serum glucagon counterregulatory hormonal response to hypoglycemia is blunted in congenital hyperinsulinism. *Diabetes* 2005;54:2946-2951

