

Obesity

The changing face of childhood diabetes: Hyperosmolar non-ketotic hyperglycaemia



Jonathan Pinkney, Consultant Physician, Royal Cornwall Hospital, Truro, and Senior Lecturer, Peninsula Medical School

Childhood obesity is in the news every day, and type 2 diabetes is being diagnosed increasingly in children. In some countries and in some high-risk ethnic groups, type 2 diabetes is already the commonest form of diabetes in childhood. In the UK, however, type 2 diabetes in childhood remains unusual,

although all those involved in the acute medical care of children, in both primary and secondary care, need to be alert to this diagnosis in all its potential manifestations.

In a recent report by Fournier and colleagues from Philadelphia (see right), hyperosmolar non-ketotic hyperglycaemia ('HONK'), a classic acute metabolic

disturbance associated with type 2 diabetes, was reported in seven children, one of whom died. HONK is typically observed in adults with type 2 diabetes, either as a disturbance present at first diagnosis, or as an acute metabolic decompensation occurring during intercurrent illnesses or in patients debilitated for other reasons. In the children described, HONK occurred as the presenting manifestation of diabetes in obese children of African-American descent.

From a practical and safety point of view, it remains essential that a diagnosis of type 1 diabetes, and therefore insulin requirement, is categorically excluded before a diagnosis of type 2 diabetes and HONK is accepted in children. The description of HONK in children is certainly a sign of our times.

PEDIATRIC DIABETES



Study supports need for increased awareness of type 2 diabetes in children

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓✓✓

- Case reports suggest that there is significant mortality associated with hyperosmolar non-ketotic hyperglycaemia (HONK) in children.
- A retrospective chart review was carried out, with the aim of providing updated information on HONK in children.
- The records of all patients at the Children's Hospital of Philadelphia who were diagnosed with type 2 diabetes over a period of 5 years (n=190) were reviewed.
- Retrospective screening was carried out for laboratory evidence of previous HONK episodes.
- The screening yielded a frequency of 3.7%; all cases were in African-American children.
- One child with HONK developed multisystem organ failure, which led to death on the fourth day of hospitalisation.
- Among the six survivors, the average time until mental status was deemed to have returned to normal was 3 days.
- The authors state that there is a need for a heightened awareness of type 2 diabetes in children, given the morbidity and mortality that is associated with HONK.

Fournier SH, Weinzimer SA, Levitt Katz LE (2005) Hyperglycemic hyperosmolar non-ketotic syndrome in children with type 2 diabetes. *Pediatric Diabetes* 6(3): 129-35

DIABETES CARE



Rosiglitazone plus insulin improves HbA_{1c} without insulin dose increase

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓✓

- No previous study had explored the potential benefit of a thiazolidinedione in type 1 diabetes.
- This double-blind study investigated rosiglitazone's safety and efficacy in 50 adults with type 1 diabetes and a baseline body mass index ≥ 27 kg/m².
- Participants were randomised for 32 weeks to insulin plus

placebo or insulin plus 4 mg rosiglitazone (insulin regimen and dosage was individualised for near-normal glycaemic control).

- The rosiglitazone group had a significant drop in HbA_{1c} ($7.9 \pm 1.3\%$ to $6.9 \pm 0.7\%$; $P < 0.0001$) without an increase in insulin dose (77.5 ± 28.6 IU/day at baseline and 75.3 ± 33.1 IU/day at 32 weeks).
- The placebo group also had a significant drop in HbA_{1c} ($7.7 \pm 0.8\%$ to $7.0 \pm 0.9\%$; $P = 0.002$), but there was a significant increase in insulin dose (74.0 ± 33.8 IU/day at baseline to 82.0 ± 48.9 IU/day at 32 weeks; $P < 0.05$).
- The authors concluded that rosiglitazone added to insulin improves HbA_{1c} without an increase in insulin dose.

Strowig SM, Raskin P (2005) The effect of rosiglitazone on overweight subjects with type 1 diabetes. *Diabetes Care* 28(7): 1562-7

NEW ENGLAND JOURNAL OF MEDICINE

Higher FPG levels within normal range predict diabetes risk

Readability	✓✓✓✓✓
Applicability to practice	✓✓
WOW! factor	✓✓✓✓

1 The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus of the American Diabetes Association has recently reduced the cut-off for 'normal' fasting plasma glucose (FPG) levels to 5.55 mmol/l.

2 Research is needed to establish whether higher FPG levels within the new normal range are an independent predictor for type 2 diabetes risk in young adults.

3 Blood measurements, physical examination data, and medical and lifestyle-related information were obtained from men in the Israel Defence Force with FPG levels <5.55 mmol/l (n=13 163; age, 26–45 years).

4 The risk of type 2 diabetes was determined using a multivariate model that adjusted for serum triglyceride levels, body mass index, age, physical activity level, family history of diabetes and smoking status.

5 Compared with men with FPG levels in the bottom quintile (<4.5 mmol/l), hazard ratios (HRs) were significant for men in the third quintile (HR, 1.82; 95% confidence interval [CI], 1.16–2.86), fourth quintile (HR, 2.64; 95% CI, 1.60–4.37) and fifth quintile (HR, 2.84; 95% CI, 1.67–4.87); this trend of progressive risk was also significant ($P<0.001$).

6 It is suggested that an individualised definition of a 'normal' FPG level, incorporating body mass index and triglyceride levels, may be of more clinical value than a single measurement of blood glucose.

Tirosch A, Shai I, Tekes-Manova D et al (2005) Normal fasting plasma glucose levels and type 2 diabetes in young men. *New England Journal of Medicine* **353**(14): 1454–62

DIABETIC MEDICINE

CSII may be superior to MDI in obese type 2 diabetes

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓

1 The aim of this randomised cross-over trial (n=40) was to compare the efficacy of continuous subcutaneous insulin infusion (CSII) with that of multiple daily injections (MDI) in obese people with type 2

diabetes who were poorly controlled on insulin therapy plus metformin.

2 In the intent-to-treat and completers' cohorts, the authors report a treatment advantage of CSII over MDI, but the only significant difference in outcome found was change in insulin dose in the completers' cohort (+20.1 IU/day with MDI and -15.5 IU/day with CSII; $P<0.0001$).

3 The authors use the findings to suggest that insulin pump therapy may have advantages in type 2 diabetes.

Wainstein J, Metzger M, Boaz M et al (2005) Insulin pump therapy vs. multiple daily injections in obese Type 2 diabetic patients. *Diabetic Medicine* **22**(8): 1037–46

DIABETES CARE

BMI associated with retinopathy and neuropathy

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 The role of body mass index (BMI) in vascular diabetes complications is unclear for type 1 diabetes.

2 The objective of this study was to investigate this role, with regard to retinopathy and neuropathy.

3 People with type 1 diabetes were divided into a group with BMI

<25 kg/m² (168 men; 146 women) and a group with BMI ≥25 kg/m² (156 men; 122 women); retinopathy was examined using fundoscopy and electromyography was used for neuropathy.

4 The group with BMI ≥25 kg/m² had significantly more retinopathy (63% versus 45%; odds ratio [OR], 2.1; $P<0.0001$) and neuropathy (49% versus 38%; odds ratio [OR], 1.6; $P=0.008$).

5 Logistic regression analysis revealed, however, that BMI was not an independent risk factor for retinopathy or neuropathy; HbA_{1c} and diabetes duration remain the major determinants.

De Block CE, De Leeuw IH, Van Gaal LF (2005) Impact of overweight on chronic microvascular complications in type 1 diabetic patients. *Diabetes Care* **28**(7): 1649–55

ARCHIVES OF DISEASE IN CHILDHOOD

Metabolic complications in childhood obesity

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓✓

1 Limited clinical resources for obesity treatment, coupled with a potentially increasing number of therapies for adolescents, suggest that the people with obesity who are most at risk of co-morbidities may need to be targeted for treatment.

2 This study aimed to identify clinical features that predicted the risk of co-morbidities in children (n=126) in an obesity clinic; 25% of those screened had evidence of the metabolic syndrome.

3 Fasting blood glucose alone was found to be unsatisfactory for evaluating glucose homeostasis. HDL cholesterol and triglycerides were related to insulin sensitivity (HOMA).

4 Parental diabetes was deemed a good predictor of impaired glucose tolerance. There was a trend for metabolic syndrome to be associated with low birthweight.

Sabin MA, Ford AL, Holly JM, Hunt LP, Crowne EC, Shield JP (2005) Characterisation of morbidity in a UK, hospital-based, obesity clinic. *Archives of Disease in Childhood* [Epub 24 October ahead of print]

'An individualised definition of a 'normal' FPG level, incorporating body mass index and triglyceride levels, may be of more clinical value than a single measurement of blood glucose [in predicting type 2 diabetes].'

'There was a trend for metabolic syndrome to be associated with low birthweight.'