Diabetes

Serious life events raise risk of type 1 diabetes in children

A recent prospective study from Sweden has shown that experiencing a serious life event during the first 14 years of life is associated with a three-fold increased risk of developing type 1 diabetes.

Families with babies born between 1 October 1997 and 30 September 1999 were invited to participate in the All Babies in Southeast Sweden (ABIS) project. Around three quarters of the target population agreed to participate and answer the questionnaire, yielding a sample population of more than 16,000 families.

Further questionnaires were completed when the children were aged 2-3, 5-6, 8 and 10-13 years. The researchers accessed 10,495 records of children included in at least one of the four data collections. Overall, 58 children were diagnosed with type 1 diabetes.

Serious life events included divorce, domestic violence, a serious illness or accident in the family, death of a relative, and either the mother or her partner becoming unemployed. In the later questionnaires there were more detailed sections on family stress and support mechanisms.

An earlier study using blood samples taken from the children at 2-3 years had established a significant association between divorce and the presence of insulin and GAD antibodies. Other sources of stress were all associated with increased antibody levels but not at statistically significant levels. The presence of these antibodies is suggestive of an increased risk of subsequently developing type 1 diabetes.[1]

This present study of the cohort confirmed that childhood experience of a serious life event overall was associated with a higher risk of future diagnosis of type 1 diabetes HR 2.84 (95% CI: 1.48-5.44; P = 0.002) when adjusted for heredity for type 1 and 2 diabetes, age at entry to study, size for gestational age, parental educational attainment, and maternal work history.

The study has been shown to underrepresent parents with low levels of education and those born overseas, but is thought to be a robust and substantial prospective data source.

This is not the first study to suggest that stressful life events may predispose to the development of type 1 diabetes, but it is the first prospective cohort study to confirm and quantify the risk.

The exact mechanism that leads to the development of type 1 diabetes remains unknown. It is thought to be multifactorial, with external stimuli acting on a genetically predisposed individual. Stress is known to alter immune function and also to result in endocrine changes that may affect insulin sensitivity and stress the beta cells of the pancreas.

It is postulated that the need for children to remain closely bonded to their parents means that parental stress is closely mirrored in their children. It is unlikely to be possible to reduce the incidence of type 1 diabetes in the future by reducing external stresses. However, the findings may provide another clue in elucidating the pathway that results in diabetes, and may alert clinicians to children who may be at higher risk.

Patients have often told me that a traumatic life event occurred shortly before the diagnosis of diabetes, so I read this research with interest.

DR MATTHEW LOCKYER

● **Nygren M, Carstensen J, Koch F et al. Experience of a serious life event increases the risk for childhood type 1 diabetes: the ABIS population-based prospective cohort study. *Diabetologia* 2015;58:1188-97**

REFERENCE

1 Sepa A, Frodi A, Ludvigsson J. Mothers' experiences of serious life events increase the risk of diabetes-related autoimmunity in their children. *Diabetes Care* 2005. doi:10.2337/diacare.28.10.2394

Obstetrics and gynaecology

Are statins safe to use during pregnancy?

A large epidemiological study from the United States on statin use in the first trimester of pregnancy has found no evidence of a teratogenic effect. However, the study authors concluded that further research is needed before statins can be considered safe in pregnancy.

A cohort of 886,996 pregnancies was collected over an eight-year period from 2000 to 2007. All the women received care exclusively on the Medicaid programme with data collection starting at least three months prior to the index pregnancy and running continuously through to at least one month following it.

A total of 1,152 (0.13%) women filled a prescription for statins during the first trimester. Data on the use of the seven statins available during the study period were collected and combined.

Data on maternal comorbidity for example hypertension, renal disease, obesity, hyperlipidaemia, and pre-existing diabetes, and tobacco, alcohol and illicit drug use were recorded.

The primary outcome was the occurrence of a congenital abnormality in the infant.

Women who used statins tended to be older and less likely to be of African-American origin. They were more likely to have comorbidities, especially diabetes and to have been exposed to oral hypoglycaemic agents.

Congenital malformations were present in 6.34% (n = 73) of the statin exposed pregnancies and 3.55% (n = 31,416) in unexposed pregnancies; unadjusted relative risk (RR) for malformations in statin-exposed pregnancies 1.79 (95% CI: 1.43-2.23). Central nervous system and cardiac

abnormalities were significantly more common in the statin-exposed pregnancies. However, after controlling for pre-existing diabetes and other confounders the RR of any congenital abnormality dropped to a statistically insignificant value, RR 1.07 (95% CI: 0.85-1.37).

Although this study provides reassurance about the use of statins in pregnancy, as with any observational study, it was open to bias and its findings offer guidance rather than proof. It seems reasonable to continue advising women not to conceive while taking statins especially as more subtle neurodevelopmental and infant behaviour effects were not addressed.

The study authors caution: 'Our analysis did not find a significant teratogenic effect from use of statins in the first trimester. However, more information about the long-term effects of in utero exposure to statins and about the effect on other neonatal outcomes, as well as replication of our findings in other large datasets with well measured information on statin use, confounders, and outcomes, are needed before statin use during pregnancy can be considered safe.'

DR CHRIS BARCLAY

● **Bateman BT, Hernandez-Diaz S, Fischer MA et al. Statins and congenital malformations: cohort study. *BMJ* 2015;350: h1035 doi: 10.1136/bmj.h1035**

Cardiovascular disease

Optimal fitness levels for cardiovascular health in adolescents

The Healthy Lifestyle in Europe by Nutrition in Adolescence (HELENA) study has identified a cardiorespiratory fitness threshold associated with a more favourable cardiovascular health profile in adolescents.

The HELENA study was a multicentre, cross-sectional study carried out in ten centres across nine European countries from 2006 to 2007. The study sample comprised 3,528 boys and girls aged 12.5-17.5 years. This fitness sub-study included 510 adolescents (259 girls).

The 20-metre shuttle run test was used to estimate cardiorespiratory fitness.

Ideal cardiovascular health was defined as meeting ideal levels of four behavioural components (smoking status, body mass index, physical activity and diet) and three health parameters (total cholesterol, blood pressure and glucose), as set out by the American Heart Association.

Higher levels of cardiorespiratory fitness were associated with a higher number of ideal cardiovascular health components in both boys and girls ($P \leq 0.001$). Levels of cardiorespiratory fitness were significantly higher in adolescents meeting at least four ideal components (13% higher in boys, $P < 0.001$; 6% higher in girls, $P = 0.008$). There was a significant discriminating accuracy of cardiorespiratory fitness. This was defined as 43.8 ml/kg/min in boys, odds ratio (OR) 6.44 (95% CI: 2.58-16.06) and 34.6 ml/kg/min in girls, OR 2.76 (95% CI: 1.32-5.78) in identifying the presence of at least four ideal cardiovascular health components.

The authors conclude that there appears to be an optimal cardio-respiratory fitness level associated with a healthier cardiovascular profile in adolescents. They go on to suggest that fitness standards could be used in schools as part of both surveillance and screening programmes to identify young people with poor health behaviour patterns who might benefit from intervention programmes.

DR PETER SAVILL

● **Ruiz JR, Huybrechts I, Cuenca-Garcia M et al on behalf of the HELENA study group. Cardiorespiratory fitness and ideal cardiovascular health in European adolescents. *Heart* 2015;101:766-773**

Sexual health

Domestic violence and termination of pregnancy

One in six women requesting a termination has suffered domestic violence during their lifetime and 4% during the current pregnancy, a study from a London clinic has found.

This study aimed to measure the prevalence of domestic violence in a population of women seeking termination of pregnancy, using a cross-sectional survey, as part of a series of preparatory studies looking at the feasibility and design of a health service intervention.

Four clinics (two NHS and two private) were approached and one provider based in London agreed to participate. The questionnaire was a modified version of the Abuse Assessment Screen which has been validated internationally. It was truncated to fit one sheet of A4 with 11 questions – five on demographics, five on abuse and one about attitudes to support services. There was also space for free text responses. The questionnaire was anonymous and completed in privacy.

Women accessing the clinic for termination between May 2012 and July 2012 were eligible for the study. Women were excluded if they were under 16, unable to speak or write English, or if the clinician felt it was not appropriate to offer them the questionnaire. A total of 383 questionnaires were given out and 190 returned, a response rate of 50%.

The questionnaire also included contact details of local support services for women in abusive relationships attached as a business card. Sixty six participants removed »

the card from the questionnaire, an uptake rate of 35%.

The mean age of respondents was 27 years (range 16 to 44) and a range of ethnicities was recorded – white British (35%), black (30%), Asian (8%), white other (13%) and other (14%). Around half (49%) of the respondents had no children. The prevalence of lifetime domestic violence was 16% and prevalence during the current pregnancy 4%.

Although there were no significant associations between domestic violence and age, ethnicity, number of children or stability of relationship; there appeared to be a higher rate of domestic violence, both lifetime and in the past year, with increasing number of terminations, but this was not statistically significant (P = 0.196).

Three quarters (133/178) of respondents were in favour of the idea of a domestic violence support service; there was no difference between those who had a previous history of domestic violence (26/35) and those who did not (107/143).

There were 64 free text comments, nine of which were from women who reported experience of domestic violence. The most common response was support for the idea of a domestic violence screening programme. Some commented that the way termination services were set up might be ideal for domestic violence intervention. Others also felt this might be a time when women might wish to seek help but three respondents disagreed, saying a specialist domestic violence setting might be more appropriate.

Although the study is limited by the relatively small sample size and low response rate and was carried out in one London clinic, it appears to be feasible and important to ask about experience of domestic violence in this cohort of women, particularly those who have had more than one termination. This question could even be asked in general practice at the time of referral when a woman presents requesting a termination.

DR RICHARD MA

● **Motta S, Penn-Kekana L, Bewley S. Domestic violence in a UK abortion clinic: anonymous cross-sectional prevalence survey. *J Fam Plann Reprod Health Care* 2015;41:128-133**

Addiction

Do anabolic steroids cause violent behaviour?

Violent offending appears to be associated with the combined misuse of multiple substances rather than anabolic androgenic steroids per se, a large study from Sweden has found.

Using data from a previous twin study (STAGE), the researchers identified 10,365 men aged between 20 and 47 years with a self-reported lifetime use of anabolic androgenic steroids.

Data on self-reported use of other illicit substances, alcohol, ADHD, and personality disorder symptoms were also collated. This information was cross-referenced with the Swedish National Criminal Conviction Register to identify any history of conviction for a violent offence for these participants.

The lifetime prevalence of anabolic androgenic steroid use reported by study participants was 0.7%, which is similar to other population studies.

There was a strong association between self-reported lifetime anabolic androgenic steroid use and conviction for a violent crime 2.7 vs 0.6% in those with a conviction compared with those without a conviction; odds ratio (OR) = 5 (95% CI: 2.7-9.3).

However, this association lost statistical significance after adjustments were made for other substance use, OR 1.6 (95% CI: 0.8-3.3).

Controlling for potential confounders such as IQ, psychological functioning, ADHD, personality disorder symptoms and childhood socioeconomic status did not lower the risk further.

Because the study sample consisted of twins, the authors had the potential to undertake co-twin control analyses to manage confounding by factors shared by twins. However, the low prevalence of anabolic androgenic steroid use in the study population rendered the statistical power too low for an informative analysis.

The use of anabolic androgenic steroid drugs together with other image and performance enhancing drugs has increased in recent years. In addition to their anabolic effects, anabolic androgenic steroids are psychoactive, and are known to influence a number of neurotransmitter systems.

Their use has been associated with effects on mood, including irritability, depression and mania. The literature has also included some suggestion of links between anabolic androgenic steroid use and criminality, aggression and violent behaviour, though research findings have not been consistent and the potential causal impact of anabolic androgenic steroids on acts of interpersonal violence has remained unproven.

The authors conclude that the data from this study demonstrate that although anabolic androgenic steroid use is more common among violent offenders, any increased risk of interpersonal violence is caused by concomitant use of substances such as benzodiazepines, amphetamines and alcohol, rather than anabolic androgenic steroid use itself.

'These findings suggest that professional assessment and treatment of violence risk should consider overall substance use patterns rather than anabolic androgenic steroid use in isolation,' they state.

DR JEZ THOMPSON

● **Lundholm L, Frisell T, Lichtenstein P et al. Anabolic androgenic steroids and violent offending: confounding by polysubstance abuse among 10 365 general population men. *Addiction* 2014:110:100–108**

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