Selected Summaries

Birth weight, early weight gain, and risk of type 1 diabetes

Harder T, Roepke K, Diller N, Stechling Y, Dudenhausen JW, Plagemann A. (Clinic of Obstetrics, Division of 'Experimental Obstetrics', Charité—Universitätsmedizin Berlin, Berlin, Germany.) Birth weight, early weight gain, and subsequent risk of type 1 diabetes: Systematic review and meta-analysis. *Am J Epidemiol* 2009;**169:**1428–36.

SUMMARY

This article examines the association of birth weight and early weight gain with subsequent risk of development of type 1 diabetes. A systematic review and meta-analysis was done according to the Meta-analysis of Observational Studies in Epidemiology (MOOSE) Group checklist, which is a consensus statement developed to improve the quality of reporting of meta-analysis of observational studies.[1] A literature search was done including the databases MEDLINE (1966–2007) and EMBASE (1989–2007) along with a manual search of all references cited in the original studies and reviews. Twelve studies were reviewed involving a total of 2 398 150 persons, including 7491 with type 1 diabetes. The odds ratios (OR) and 95% confidence intervals (CI) of type 1 diabetes associated with birth weight were calculated. Three different approaches were used for analysis. First, a birth weight cut-off of 4000 g (high birth weight) was used to compare the risk of type 1 diabetes below and above this value (dichotomous comparison). Second, a birth weight cut-off of 2500 g (low birth weight) was used to compare the risk of type 1 diabetes below and above this value. Third, the 'pool-first method' was used to combine regression coefficients obtained from the studies (linear trend analysis). Fixed-effects and random-effects models were fitted wherever relevant. Heterogeneity assessment was done by the Cochrane Q-based test and the I^2 calculation. Sensitivity analysis (by 4 different subgroup analyses), influence analysis, analysis of confounder adjusted data and assessment of publication bias (by inspection of funnel plot, Begg test and Egger test) were also done. Meta regression analysis was also done to check for the presence of any cohort effect.

High birth weight was found to be associated with increased risk of type 1 diabetes, with identical effect sizes with random- and fixed-effects models (OR 1.17, 95% CI 1.09–1.26). No significant heterogeneity was observed. Sensitivity analysis and influence analysis showed no remarkable effect on the pooled estimate. Analysis of confounder-adjusted data was done in 6 studies; the association was found to be stronger than in the unadjusted analysis (OR 1.43, 95% CI 1.11–1.85). The analysis of association of low birth weight and type 1 diabetes was possible in 8 studies. Low birth weight was associated with a non-significantly reduced risk of type 1 diabetes (OR 0.82, 95% CI 0.54–1.23) with the random-effects model, and significantly reduced risk (OR 0.56, 95% CI 0.51–0.61) with the fixed-effects model; with significantly heterogeneous ($p<0.001$) single study values and an I^2 of 91. Influence analysis showed that no study had a strong influence on the pooled estimate. Linear trend analysis was possible in 9 studies. Each 1000 g increase in birth weight was found to be associated with a non-significant 7% increase in the risk of type 1 diabetes (OR 1.07, 95% CI 0.99–1.15). Results were significantly heterogeneous and influence analysis showed that omission of a particular study changed the pooled OR towards significance (OR1.10, 95% CI 1.03–1.18). No evidence of publication bias was found. For analysis of association of weight gain during the first year of life and risk of type 1 diabetes, 4 studies were available, with 3861 individuals, including 1266 with type 1 diabetes. Quantitative summarization of findings from these 4 studies was not possible, due to differences in exposure measurement and description of weight gain.

The authors concluded that high birth weight and increased early weight gain are risk factors for type 1 diabetes, although evidence for the latter is limited.

COMMENT

As per the International Diabetes Federation report published in 2007, of the world's 1.8 billion children below 14 years of age, approximately 440 000 had type 1 diabetes, representing a prevalence of 0.02% (20 per 100 000 persons). The annual incidence of type 1 diabetes in Southeast Asia was <4 per 100 000 persons, comparatively lower than in the western world.[2] The data on type 1 diabetes in India are limited. In one study, the prevalence of type 1 diabetes was reported to be 10.6 per 100 000 persons below 20 years of age.[3] The results of another recent study put the prevalence at 10.2 per 100 000 persons below 16 years of age, with a higher prevalence in urban (26.6 per 100 000 persons) compared with rural areas (4.27 per 100 000 persons).[4] According to the Karnataka Diabetes Registry, from the year 1995 through 2008, the overall incidence of type 1 diabetes was 3.8 per 100 000 persons, and the incidence of type 1 diabetes was showing a rising trend.[5]

So, though the incidence rates of type 1 diabetes in Southeast Asia remain low, the actual number of children affected is considerable, given the large population base. This is especially true for India, with more than a quarter of the population being <15 years of age—the age mostly affected by type 1 diabetes.[6]

This study provided further evidence that high birth weight is associated with a higher risk of type 1 diabetes. In India, although low birth weight is still the major issue, there is enough evidence to suggest that women from an urban background give birth to babies with birth weights much higher than their rural counterparts and almost at par with babies born in the West.[7] The proportion of low birth weight among urban mothers is also comparatively lower.[8] With the burden of type 1 diabetes being more in urban than rural India,[4] the findings of this study become particularly relevant.

However, the results of this study need to be interpreted with caution. To start with, the authors restricted their electronic search to the Excerpta Medica database, EMBASE, to the years 1989 to 2007 only, whereas articles in the database can now be searched electronically from 1947 onwards. Thus, the investigators might have missed some relevant studies. In the two studies by Stene *et al.*, the larger study may have included participants from the smaller study as well.[9,10] This might have caused the heterogeneity to go down spuriously. For sensitivity analysis, in all categories except study design, subgroup analyses provided non-significant results in one or the other subgroup. Though there is not much difference in the effect sizes from the overall pooled estimate in

any subgroup, any further comparison and interpretation on the basis of these non-significant results is invalid. The authors concluded that early weight gain is a risk factor for type 1 diabetes. However, quantitative summarization of findings from the 4 available studies providing data on weight gain was not done, on account of the differences in methodology in the studies. All that was possible was a systematic review. Thus, the evidence accumulated from the 4 studies cannot be said to have been generated from this particular study.

This meta-analysis substantiates the evidence generated by previous studies on the association between high birth weight and type 1 diabetes. This is important in the context of growing urbanization and increasing incidence of type 1diabetes. Screening of high birth weight babies will facilitate early diagnosis of type 1 diabetes. As demonstrated in the Diabetes Control and Complications Trial and its long-term follow up study, the Epidemiology of Diabetes Interventions and Complications trial, appropriate glycaemic control at an early stage significantly reduces the risk of vascular complications.[11–14] Early diagnosis and management of type 1 diabetes effectively delays the onset and slows the progression of diabetic retinopathy, nephropathy and neuropathy.

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Exploring alternative health services for HIV screening of high risk individuals

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SUMMARY

Visits to dental clinics are more frequent than to integrated counselling and testing centres (ICTCs). The authors explored the opportunity for dental healthcare providers to screen their patients for HIV. Oral fluid can be tested for HIV. This simple and minimally invasive test, which gives results in 20 minutes, is highly sensitive, specific and cost-effective. The researchers used data from the United States 2005 National Health Interview Survey (NHIS) to investigate whether persons at self-identified risk for HIV visit dental clinics. They also explored whether dental clinics reach at-risk persons who have not been tested in other clinical settings. NHIS, a large, nationally representative survey of the US population, is conducted annually. The survey includes self-reported information on healthcare utilization including visits to dental offices and recent HIV testing. The authors correlated visits to a dental clinic with income, education, race, religion and health insurance coverage. Adult respondents were asked about their chances of getting infected with HIV. Those who answered 'high' or 'medium' were further asked about recent HIV testing. Respondents were also asked if they were exposed to any of the following HIV risk factors: receipt of anti-haemophilia clotting factors, men who have sex with men, injection drug use, commercial sex work or having sexual relations with those having known HIV risk factors. Of the sample population, 8.7 million (4%) were found to be at self-reported risk for HIV infection. Of these, more than one-third had never been tested for HIV. In the majority of those who had ever been tested, the test was done >5 years ago. Around 6.5 million (74%) HIV-exposed persons had visited a dental care setting at least once in the preceding 2 years. Of those who reported being at risk for HIV infection, and who had never been tested or had not been tested in the past 5 years, >70% had seen a dentist within the past 2 years of the interview. To identify subpopulations of high risk individuals who were especially promising for HIV testing, two models of multivariate logistic regression were tested. The researchers obtained similar results in both models where dependent variables were individuals who reported facing HIV risk, had never been tested for HIV and had seen a dentist in the past 2 years, and individuals who