International parallels in leukaemia and diabetes epidemiology

R G Feltbower, P A McKinney, M F Greaves, R C Parslow, H J Bodansky

Acute lymphoblastic leukaemia (ALL) and type 1 diabetes have an environmental aetiology and common epidemiological features. Incidence rates and national characteristics of both conditions were investigated in 40 countries worldwide. There was a significant positive correlation between the diseases. Markers of wealth and affluence were significantly associated with high incidence.

Methods

Firstly we tested for correlations in international incidence of childhood ALL and type 1 diabetes (ages 0–14); secondly we explored factors that might explain variation in rates. The correlation (Pearson’s product moment test) in rates across 40 countries was investigated by taking comparable published temporal and geographical data on standardised incidence rates. Where rates were only available for parts of countries, those from the same nation were pooled using weights based on case frequencies. For example, one sub-area with an overall rate based on 1000 individuals would carry twice the weight as a second sub-area containing 500 individuals.

Results

The analysis showed a significant positive correlation between the incidence rates of ALL and type 1 diabetes ($r = 0.53$, $95\%$ CI 0.36 to 0.72) (fig 1). This pattern was similar across Europe ($n = 26$) and the rest of the world ($n = 14$) and the exclusion of Finland as the only outlier made no difference to the results.

Higher rates of diabetes are associated with wealth and affluence in European countries, so we tested for associations with diabetes worldwide and for the first time explored the relation between levels of national prosperity and ALL incidence. The explanatory variables were gross domestic product (GDP), infant mortality, and life expectancy. Additional factors previously linked to disease incidence were examined including population density (linked to diabetes and ALL), coffee consumption (diabetes), and cows’ milk consumption (diabetes). A recently suggested potential protective effect from vitamin D supplementation in early life for type 1 diabetes was indirectly measured by examining latitude and average hours of sunshine.

The logarithmic or reciprocal transformation was used for factors which were highly skewed (GDP, infant mortality and population density; table 1). The remaining explanatory variables and incidence rates themselves were all reasonably normally distributed. Correlations and separate linear regression models were applied to each disease, with each factor included as an independent variable. All statistical analyses were performed using Stata.

The correlation and regression analyses showed positive associations for GDP, infant mortality, and life expectancy with both ALL and type 1 diabetes (table 1).

Discussion

Our analysis clearly shows for the first time that the international incidence of ALL and type 1 diabetes are positively associated. Countries with either high or low incidence of either disease are likely to have a corresponding rate of the other condition.

Markers of national prosperity appear to explain some of the worldwide variation between countries for both ALL and type 1 diabetes, which is consistent with observations in European populations. The same links with socioeconomic variables can also be seen within countries at a smaller geographical scale. Exactly what specific “affluent” lifestyle
Table 1  Correlation and parameter estimates from linear regression for standardised incidence rates of childhood acute lymphoblastic leukaemia and type 1 diabetes from 40 countries for specific national characteristics

<table>
<thead>
<tr>
<th>Factor</th>
<th>Type 1 diabetes</th>
<th>Leukaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Correlation</td>
<td>Adjusted R²</td>
</tr>
<tr>
<td>Gross domestic product (1994, US$ per head)</td>
<td>0.60 (0.47 to 0.72)</td>
<td>0.11</td>
</tr>
<tr>
<td>Infant mortality (1995, per 1000 live births)</td>
<td>0.45 (0.30 to 0.60)</td>
<td>0.15</td>
</tr>
<tr>
<td>Life expectancy (1995)</td>
<td>0.41 (0.27 to 0.56)</td>
<td>0.006</td>
</tr>
<tr>
<td>Sunlight (average hours per day)</td>
<td>0.38 (0.25 to 0.51)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Pearson's product moment correlation coefficient.

Logarithmic transformation used; inverse transformation used.

also in relation to temporal trends. The striking parallels in the descriptive epidemiology of type 1 diabetes and ALL in children suggest that an exploration of common causal pathways linked to the immune response in early life and underlying genetic susceptibility in individuals would be fruitful.

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