Risk of Congenital Malformations and Environmental Pollution in Lombardy

Rischio di malformazione congenita
e fonti di inquinamento ambientale in Lombardia

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Riassunto: Nel lavoro viene condotta un’analis i territoriale delle malformazioni congenite alla nascita in Lombardia con il duplice scopo di produrre una mappa di rischio - tutt’oggi assente in letteratura - e di mettere in relazione le aree a maggiore incidenza con potenziali fattori di inquinamento ambientale. I dati utilizzati riguardano tutte le nascite che hanno avuto luogo in Lombardia nel periodo 1994-96 (schede Istat D1 e D2).

L’analisi viene condotta su dettaglio territoriale comunale tramite un modello bayesiano gerarchico di tipo CAR (Conditional AutoRegression). La stima viene effettuata ricorrendo a metodi MCMC. L’analisi evidenzia un significativo aumento del rischio delle malformazioni congenite nei comuni in cui è presente una fonte di emissione di sostanza inquinata ed un clustering territoriale del fenomeno considerato.

Keywords: Congenital malformation, Air pollution, Spatial epidemiology

1. Introduction

Congenital malformations (CM) are organ defects (anomalies) existing at birth. The aim of this study is twofold. First we produce a map of the risk of CM in Lombardy at the municipality level which, up to our knowledge, is still lacking in the literature. Second, we investigate the possible association between CM and industrial pollution sources.

“The health risks posed by this pollution sources are only recently being investigated”. While other adverse pregnancy outcomes, especially low birth weight and preterm birth, have been largely investigated in relation to air pollution, there are hardly any studies of the association between air pollution and risk of CM. The risk of several common birth defects may be influenced by the exposure to environmental contaminants, “mechanistically, air pollutants could be involved in the aetiology of birth defects via hemodynamic, anoxic events, oxidative stress, and toxicity to certain cell populations during development” (Beate et al., 2002, pg. 2).

In this paper, focussing on the most industrialised Italian region, we investigate the relationship between air pollution and the risk of malformation. In particular we consider 10 industrial pollution sources which produced ambient air pollutants - such as NOx (nitrogen oxide) and SO2 (sulphur dioxide) - indicated by the Ministero dell’Ambiente, as having a potential impact on public health (European directive 2001/80/CE).
2. Data

Our data are a large dataset (N = 217000) providing detailed information on births registered in Lombardy from 1994 to 1996. This is the last dataset which provides this sort of information, since the criteria for surveys of births have been recently changed. The most relevant dimensions for our study are: the presence of congenital malformation (CM) and some maternal characteristics such as the mother age at childbirth, her education, place of residence and consanguinity with the father. CM is defined as any congenital defect (with no further specification regarding the type) diagnosed at the time of birth.

The main advantage of this dataset is the high number of cases available, which makes possible reliable territorial estimates at the municipality level.

3. Statistical methods

For modelling malformation occurrences at the municipality level in Lombardy a Poisson generalized linear mixed model is used. Two random effects are included in the model in order to allow for overdispersion of counts: a spatially unstructured component (u in what follows) and a spatially structured component (s in the following) which takes into account spatial similarities amongst neighbouring areas.

The model is specified in a fully hierarchical Bayesian framework. In particular the prior for the unstructured random component is a normal distribution whose variance is inversely related to the number of children born in the municipality (borni). For the structured spatial random effect an intrinsic CAR prior is used (Besag et al. 1991). The explanatory variables entered into the model are: the standardized proportions of consanguine couples in the municipality (CON), the proportion of mothers with high educational level in the municipality (EDU; women with high educational level are those who achieved at least a high school degree) and, finally, the proportion of mothers in the area aged 40 or more (AGE). These variables are transformed in order to make them centred at the mean. Environmental sources of risk are accounted by entering in the model a binary variable (ENR) representing the presence of industrial plants with relevant emissions of NOx and SO2 (reference categories are those municipalities where no industrial plants are present). Assuming λi to be the expected frequency in municipality i, the considered model is:

\[ \log(\lambda_i) = \log(\text{born}_i) + a + b \cdot \text{CON}_i + c \cdot \text{EDU}_i + d \cdot \text{AGE}_i + e \cdot \text{ENR}_i + u_i + s_i. \]

As we mentioned above, we assume \( u_i \sim N(0, \sigma_u^2/\text{born}_i) \) and \( S_i | S_j(\delta) \sim N(\bar{s}_\delta, \sigma_s^2/n_i) \) where \( \bar{s}_\delta \) is the mean of the random component in the areas adjacent to area i and \( n_i \) is the number of adjacent areas to area i. For the fixed effects \( (a,b,c,d,e) \) non-informative but proper 0-mean normal priors with a large variance \( (10^5) \) are specified. Finally, gamma inverse priors are used for the variance parameters of the random effects, namely an \( IG(0.001,0.001) \) for the variance \( \sigma_u^2 \) of the unstructured spatial component and an \( IG(0.5,0.0005) \) for the variance \( \sigma_s^2 \) of the spatially structured
component (Kellsall and Wakefield, 1999). The model is estimated via Gibbs sampler using WinBUGS (the code is available from authors on request).

4. Results

Table 1 shows the estimates of the parameters of the model. Only for two of them we found a one-sided 90% credibility interval above 0 suggesting a statistically relevant positive effect on the risk of CM. The two variables are consanguinity and the presence in the area of industrial sites with relevant emissions of NOx and SO2. Both effects, contribute to increase the risk with respect to the baseline (the risk at baseline being 4.5‰). As far as the effect of consanguinity is concerned, it is well known that this is a potential cause of malformation, therefore, our result is consistent with a large epidemiological medical literature. Focussing on the presence of an industrial site, we found that the risk of CM is nearly 40% higher in those municipalities where an industrial plant is present. As far as the spatial dynamics of CM is concerned, the map reported in figure 1 shows the estimated malformation rates. It appears that the risk is particularly high in the northern, close to the Alps, and in the central part of the region (the province of Bergamo).

Table 1: Posterior estimates based on 15,000 iterations (5,000 burn-in)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>(SD)</th>
<th>90% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-5.404</td>
<td>(0.048)</td>
<td></td>
</tr>
<tr>
<td>CON</td>
<td>0.077</td>
<td>(0.057)</td>
<td>*</td>
</tr>
<tr>
<td>EDU</td>
<td>-0.057</td>
<td>(0.048)</td>
<td></td>
</tr>
<tr>
<td>AGE</td>
<td>0.047</td>
<td>(0.080)</td>
<td></td>
</tr>
<tr>
<td>ENR</td>
<td>0.292</td>
<td>(0.221)</td>
<td>*</td>
</tr>
<tr>
<td>$\sigma_u$</td>
<td>0.538</td>
<td>(0.128)</td>
<td></td>
</tr>
<tr>
<td>$\sigma_s$</td>
<td>0.085</td>
<td>(0.055)</td>
<td></td>
</tr>
</tbody>
</table>

5. Conclusion

In this paper we obtained two main results. First we produced a map at the municipality level of the risk of CM in Lombardy until now lacking in the literature. We identified some regular patterns in the spatial dynamic of the risk of malformation with the Northern and the central part of the region being of higher risk. Secondly, we investigated potential determinants of CM. In addition to a well known effect of consanguinity of parents on CM, we found some evidences of a positive impact of pollution, NOx and SO2 in particular, produced by industrial sources. It is important to observe, however, that we are not able to identify different kind of CM with the data at hand. Therefore it might be possible that industrial pollution sources may have even a stronger impact on some specific congenital anomalies. Furthermore
we are not able to distinguish between the two pollutants (i.e. NOx and SO2) therefore we cannot assess which of the two factors is the most relevant in affecting CM.

**Figure 1:** Estimated rates (‰) of malformation in Lombardy

![Map showing estimated malformation rates in Lombardy](image)

**References**


