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SHORT COMMUNICATION

Geographical variations in the risk of adverse birth outcomes in Spain

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Abstract The objective of this study was to describe the spatial risk-patterns of prematurity and low birth weight in Spain. A descriptive spatial analysis of births registered in the Spanish Vital Statistics during 2004–2008 using municipalities as the observation unit was carried out. Besag-York-Mollié autoregressive spatial models were adjusted using the Integrated Nested Laplace approximation to calculate relative risks and posterior probabilities of having very and moderate preterm or low weight newborns. Results were represented in maps to assess geographic risk-patterns. Spatial analysis shows geographical variations in the risk of adverse reproductive outcomes in Spain highlighting three main high-risk zones, namely, municipalities in Asturias, Madrid City and Murcia. The specific risk patterns identified on each zone suggests some differences regarding the potential underlying risk factors and specific areas for future research. A differential exposure during pregnancy to some risks potentially related to industry or agriculture and other contextual factors could underlie an unequal vulnerability to adverse reproductive outcomes in some Spanish regions.

Keywords Adverse birth outcomes · Spatial distribution · Geographical variation · Maps · Low birth weight · Preterm birth

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Introduction

Poor prenatal development is an important predictor of differences in survival, and morbidity among newborns and these differences may persist throughout life, resulting in a wide range of physical and cognitive disabilities and chronic health problems. Epidemiological studies on reproductive health have focused largely on individual-level risk factors. However, researchers increasingly point out to social and environmental factors as major contributors to the risk of adverse reproductive outcomes. In the last years, studies using spatial statistical methods and geo-visualization techniques have provided relevant epidemiological information on geographical disparities in health related to contextual factors (Sohel et al. 2010; Ugarte et al. 2010; Westercamp et al. 2010; Pedigo et al. 2011). However, in the realm of reproductive health, research studies using this approach are still scarce (Crosse et al. 1997; English et al. 2003; Cromley and Cromley 2009; Bloch 2011; Kirby et al. 2011). We carried out a spatial analysis to explore geographical patterns in the distribution of risk

Fig. 1 Geographical distribution of the average birth rate (births/1,000 inhabitants) in Spanish municipalities during the period 2004–2008

of prematurity (PTB) and low birth weight (LBW) in Spain.

Materials and methods

A database with all live births registered in the period 2004–2008 was obtained from the Spanish Vital Statistics registry. This database included information about gestational age and weight of the newborns and about mother's municipality of residence. The total birth rate for the whole period was represented in a municipality map of Spain. This rate was calculated as a weighted average of the annual ratio between the number of births observed and the population size at the end of the year.

We classified births in: very preterm birth (VPTB:<33 weeks of gestation); moderate preterm birth (MPTB:33–36 weeks of gestation); very low birth weight (VLBW:<1,500 g); and moderate low birth weight (MLBW:1,500–2,500 g). Data on singleton births were aggregated to a municipal level for the 8,098 municipalities of the Spanish territory. Assuming that the observed number of VPTB, MPTB, VLBW and MLBW cases in each municipality followed a Poisson distribution, smoothed relative risk (RR) and posterior probabilities (PP) of such RR > 1 were calculated for each outcome and municipality by fitting Besag-York-Mollié autoregressive spatial models (BYM) (Clayton and Kaldor 1987; Besag et al. 1991) using the integrated nested Laplace approximation (INLA) (Rue et al. 2009).

The BYM model for a given outcome was formulated as follows:

$$O_i \sim \mathrm{Po}(E_i \lambda_i) \quad i = 1\ldots 8{,}098$$
$$\log(\lambda_i) = \alpha + h_i + b_i$$

$$h_i \sim \mathrm{Normal}(\mu,\ \tau_h)$$
$$b_i \sim \mathrm{Car.Normal}(\eta_i,\ \tau_b)$$

$$\tau_h \sim \mathrm{Gamma}(\alpha, \varphi)$$
$$\tau_b \sim \mathrm{Gamma}(\gamma, \delta)$$

where λ_i represents the RR in municipality i, O_i represents the number of observed cases of the outcome in area i, E_i represents the expected number of cases of the outcome in area i, h_i represents a random effect capturing spatially unstructured heterogeneity, b_i represents a random effect

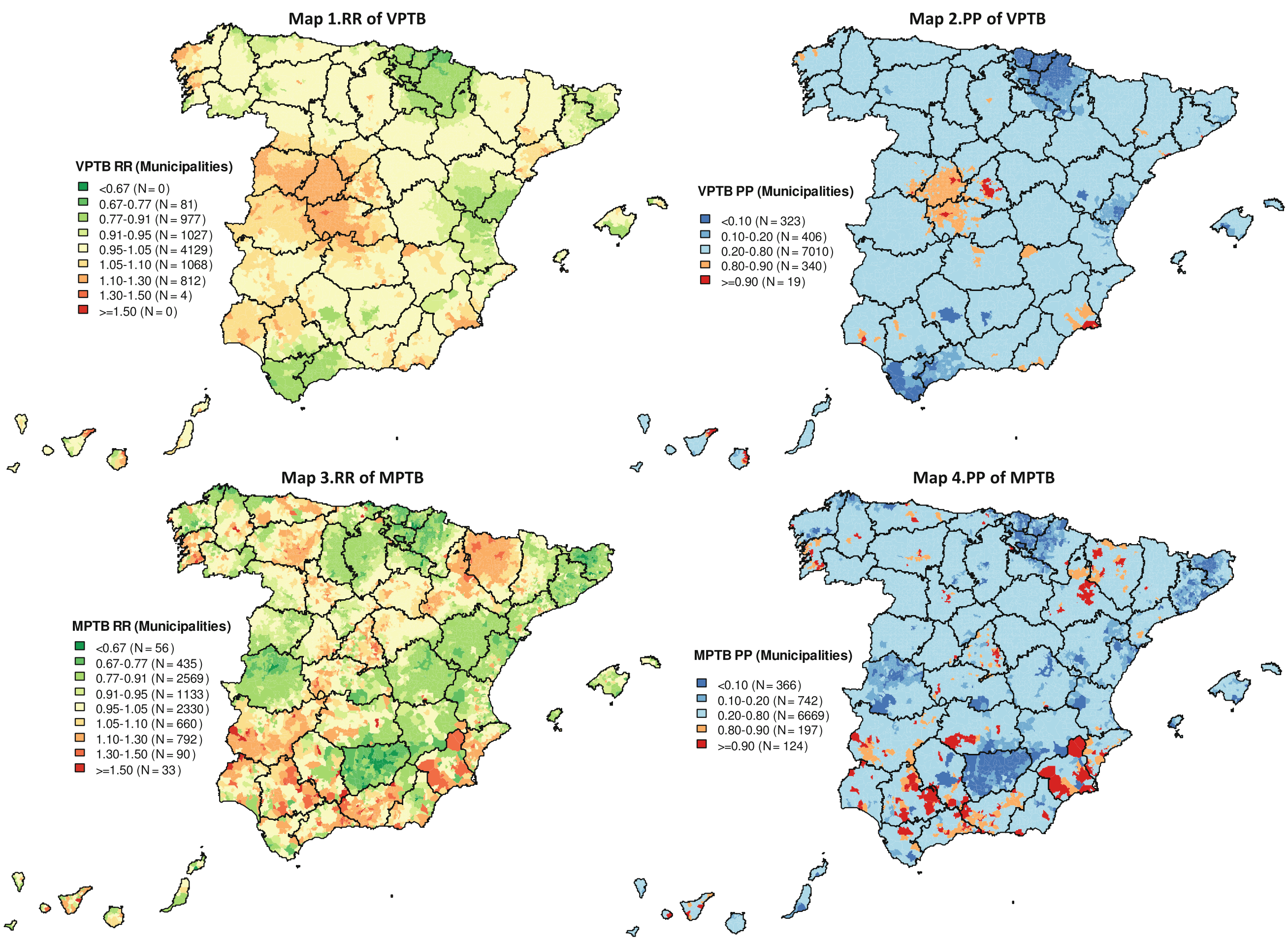

Fig. 2 Geographical distribution of smoothed relative risk (RR) and posterior probability (PP) of very (VPTB) and moderate (MPTB) preterm birth in Spain during the period 2004–2008

capturing spatially structured heterogeneity, τ_h and τ_b are the hyper parameters representing prior variance components associated with the two random effects.

So, the expected value of the spatial random effect for each municipality is an average of such effect in the contiguous municipalities. Given the irregularity in the size and shape of Spanish municipalities, the adjacency matrix was calculated defining neighbors as those sharing a boundary.

The expected number of cases for each municipality and outcome of interest was calculated as:

$$\text{Expected}_i = \text{National Raw Rate of Outcome} \times \begin{matrix}\text{Number Live}\\ \text{Births Municipality}_i^*\end{matrix} \quad i = 1\ldots 8{,}098$$

Where the national rate was defined as:

$$\text{National Raw Rate of Outcome} = \frac{\text{Number of Cases of Outcome}}{\text{Number of Live Births}^*} \times 1000$$

*With complete information about the outcome of interest.

Relative risk and posterior probabilities were depicted in Spanish municipal maps. The smoothed maps of RRs enable homogeneous areas to be delimited and PP maps allow determining which municipalities appear to have significantly RR > 1. The convention was followed, and regions were identified as having a high probability of excess risk when PP ≥ 0.8 (Richardson et al. 2004). Both RR and PP were represented in choropleth maps of Spanish municipalities using Geographical Information Systems (GIS) and a modified version of the Spanish Vital Statistics cartography of 2004. April 4, 2011 version of INLA with the option of Gaussian estimation of the parameters and the standard central composite design (ccd) approach was used as the integration strategy (Rue et al. 2009).

Results and discussion

During the period 2004–2008, 2,319,555 singleton live births were registered in the 8,098 municipalities of the Spanish territory.

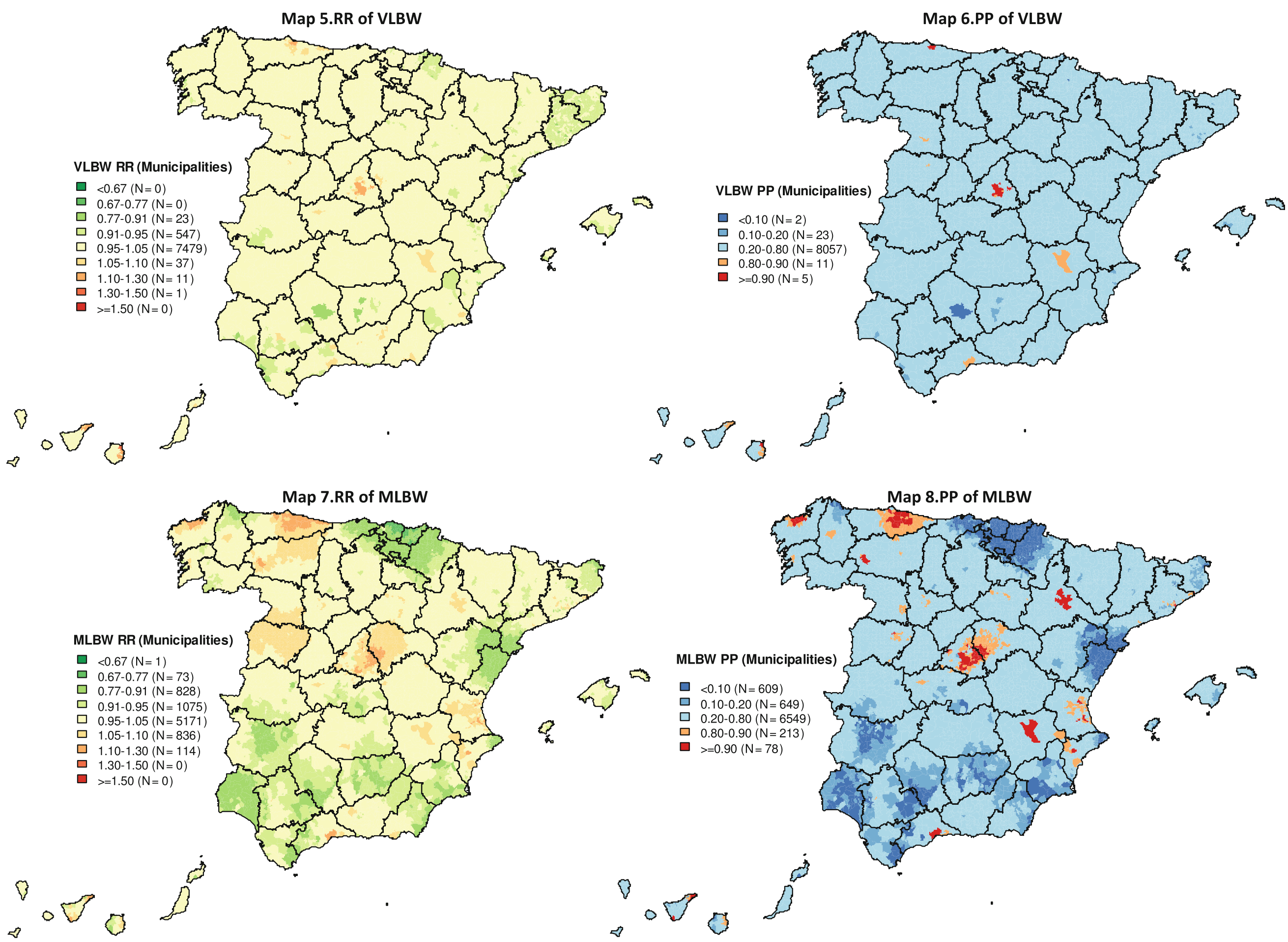

Fig. 3 Geographical distribution of smoothed relative risk (RR) and posterior probability (PP) of very (VLBW) and moderate (MLBW) low birth weight in Spain during the period 2004–2008

Figure 1 shows the spatial distribution of the average birth rate during the whole period. The mean birth rate was 10.50 births per 1,000 inhabitants. However, this estimation is a result of an average of birth rates distributed very unequally among the Spanish territory. While most of the municipalities of Madrid, provinces from south, east coast and north-east of Spain show high birth rates, the majority of municipalities from north-center and north-west Spain seem to have birth rates considerably below the national average.

Data on gestational age and birth weight were missing for 15.17 and 4.71 % of births, respectively. These data were assumed to be missing at random, and the rates for each municipality were estimated using the available information. National prevalence of very and moderate preterm birth was 0.95 and 5.24 %, respectively, while 0.60 and 5.07 % of newborns had very and moderate LBW. In Figs. 2 and 3, maps show homogeneous areas in terms of risk (smoothed RRs) of prematurity and LBW and identify specific regions with a significantly high risk ($PP > 0.8$) for each one of the four outcomes. On the Map 1, it can be identified a big area in the middle of Spain and also some isolated zones in the rest of the country with RR of VPTB between 1.10 and 1.30. However, as the Map 2 shows, only Madrid City and some municipalities in Toledo, Avila, Murcia and Huelva and in isolated points of Tenerife and Gran Canaria had a significantly high risk ($PP > 0.9$) of VPTB. Maps 3 and 4 show high RR and high PP of MPTB focused mainly in several localities of the South and especially concentrated again in Murcia region. Regarding the distribution of the risk of LBW, Map 5 and 6 identified an excess RR of VLBW between 1.10 and 1.30 with $PP > 0.9$ in Madrid City, but also in a specific point in Asturias. Finally, Maps 7 and 8 show an excess risk of MLBW in Madrid City and surroundings as well as in some localities in Asturias and in very isolated areas in the North and in the South of Spain not including Murcia region.

This study provides new data about geographical differences in the risk of prematurity and LBW in Spain. Overall, our results highlight three main high-risk zones of these adverse birth outcomes, namely, municipalities in

Asturias, Madrid City and Murcia. A concentration of high-risk areas of MPTB was found in the south of Spain. Dissimilarities in the patterns identified may suggest some differences regarding potential underlying risk factors.

Localities in Asturias showed high risk of VLBW or MLBW but no high risk of prematurity. Inversely, localities in Murcia showed high risk of very or moderate prematurity, but no high risk of LBW. Previous studies have suggested a differential distribution of preterm and LBW across regions, pointing toward deprivation as one of the main risk factors (English et al. 2003; Bloch 2011; Kirby et al. 2011). However, it has been shown that local factors other than socioeconomic may be important when identifying risks factors for prematurity and low birth weight (Crosse et al. 1997; Walsh et al. 2010). On the other hand, some studies have suggested a possible association between residential proximity to industries and adverse birth outcomes (Morgan et al. 2004; Ahern et al. 2011; Castello et al. 2013). In this sense, it could be useful to consider the remarkable disparity between Asturias and Murcia in terms of industrial activity to assess the significance of the differences found and potential risk factors associated. Asturias is a region strongly dedicated to coal mining and iron and steel industry. By contrast, Murcia hosts the largest concentration of greenhouses in Europe, most of the population been involved in agricultural activities.

Regarding Madrid City, the risk for VPTB seemed concomitant with a high risk of low birth weight, but no risk of MPTB was identified. We explored the data to explain this lack of coincidence between the spatial distribution of prematurity and low birth weight, and we observed that 48 % of VPTB cases had a birth weight over 1,500 g (above VLBW category) with a median gestational age of 32 weeks (upper limit of VPTB category) and that 58 % of MPTB deliveries showed a weight at birth above 2,500 g and had a median gestational age of 36 (upper limit of MPTB category). These data also suggest that severe prematurity is the main problem being very or moderate low birth weight partially a consequence.

These results must be interpreted considering some limitations. A recent study was carried out to validate the reliability of the gestational age and birth weight data of the Spanish Vital Statistics registry (Rio et al. 2010). However, missing data could be distorting our results if most cases correspond to smaller or more premature babies. To check this possibility, we calculated the distribution of weight among babies with missing data for gestational age and only 4.51 % were LBW babies (0.42 % VLBW). Among babies with missing data for birth weight, only 3.22 % were low preterm babies (0.74 % VPTB). In consequence, missing-at-random appears to be a reasonable assumption.

Conclusion

This exploratory study suggests that a differential exposure during pregnancy to some risks potentially related to industry or agriculture, and other contextual factors could underlie an unequal vulnerability to adverse reproductive outcomes in some Spanish regions. Further studies to explore the association between these results and environmental and socio-demographic factors are required.

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