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Ecological analysis of the relationship between infant mortality and cardiovascular disease mortality at ages 45–69 in the Brazilian 1935 birth cohort

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ABSTRACT

Background. International ecological studies have shown a positive association between infant mortality as a proxy for low birth weight and cardiovascular disease mortality in adult life.

Methods. Mortality rates due to Cardiovascular Diseases (CVDMR) standardised by age in adults between 45 and 69 years of age and by place of birth (pob) and residence (res) were related to Infant Mortality Rates (IMR) in the Brazilian 1935 birth cohort.

Results. Two relationship patterns were noted between IMR and CVDMR: for the Southeast, South and Centre-West group of regions ($r_{pob} = 0.46$; $r_{res} = 0.29$) and for the North and Northeast group of regions ($r_{pob} = 0.21$; $r_{res} = 0.33$). For the latter pattern, two states were identified (Rio Grande do Norte and Paraíba) as atypical areas, whose exclusion strengthened the association ($r_{pob} = 0.73$; $r_{res} = 0.91$).

Conclusions. The direction of the associations changed after the analysis by group of Brazilian regions (indirect control of socio-economic levels, coverage and quality of the information). There is a positive, although weak association between IMR and CVDMR. Attempts to control or minimise the interference of migratory movements, cohort effects and socio-economic levels represented methodological progress in ecological analyses of foetal programming in Brazil.

Introduction

During the 1980s, Barker (1998) developed the foetal programming hypothesis, postulating that intra-uterine malnutrition causes permanent changes in the structure, physiology and metabolism of the foetus, with life length consequences. The first indication that coronary disease may be related to shortfalls in foetal growth arises from the positive relationship between coronary disease mortality rates and mortality rates in new-borns observed in different parts of England and Wales (Barker and Osmond, 1986). The association between infant mortality and low birth weight (intra-uterine malnutrition marker) in the past is known and consequently, the infant mortality rate was construed as a proxy for low birth weight (Barker, 1995).

In Brazil, mortality rates due to acute myocardial infarction in the Northeast and South regions in 2000 and infant mortality rates between 1930 and 1950 were not shown to be related (Alves and Figueiroa, 2004). Some methodological constraints may have contributed to such finding, including the few geographical units under analysis, the internal heterogeneity of the populations and, aligned with other foetal programming studies, waves of migration (Fang et al., 1996; Osmond et al., 1990) cohort effects (Baker et al., 1993; Pringle, 1998), confounding (Owen et al., 2005) and because population risks are determinant factors not necessarily valid at the individual level (Owen et al., 2005; Rose, 2001).

This study investigated the ecological relationship between infant mortality rates and cardiovascular disease mortality rates at ages 45 to 69 in the Brazilian 1935 birth cohort.

Methods

Based on available data, 18 Brazilian states were selected for analysis, being classified into five geographical regions: North (Amazonas and Pará); Northeast (Alagoas, Bahia, Ceará, Maranhão, Paraíba, Pernambuco, Piauí, and Rio Grande do Norte); Southeast: (Espírito Santo, Minas Gerais and São Paulo), Centre-West (Goiás and Mato Grosso); and South (Paraná, Rio Grande do Sul and Santa Catarina).

The infant mortality rate (IMR) calculated for the period between 1930 and 1940 was referred to its mid-point year, corresponding thus to the 1935 birth cohort (IBGE, 1986). Data on cardiovascular mortality in adult life

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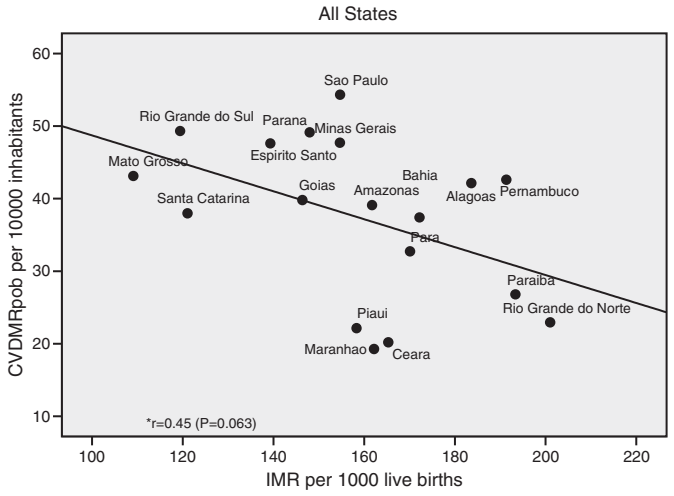

Fig. 1. Mortality rate distribution by cardiovascular disease at age 45–69, standardised by place of birth (CVDMRpob) and infant mortality rates (IMR) in the 1935 Brazilian birth cohort.

(encompassed by the International Statistical Classification of Diseases Chapter on Diseases of the Circulatory System) were obtained from the Mortality Information System (MS, 2009), by place of birth (pob) and state of residence (res), for the following three-year periods: 1979/1980/1981, 1990/1991/1992 and 1999/2000/2001. Population data were obtained from the 1980, 1991 and 2000 Demographic Censuses (IBGE, 1984; IBGE, 2009).

Cardiovascular disease mortality rates per 10,000 inhabitants (CVDMR) were calculated for the 1935 birth cohort for age and the year in which death occurred, at ages 45 to 49 years from 1979 to 1981, 55 to 59 years from 1990 to 1992, and 65 to 69 years from 2000 to 2002. The total CVDMRs (45 to 69 years) were standardised by the direct method (Szklo and Nieto, 2007), taking the population of São Paulo State in 2000 as the standard.

The relationship between IMR and CVDMR in the 1935 birth cohort (pob and res) was analysed using scatter plots and Pearson's linear correlation coefficients (r).

Results

The IMR varied between around 109 (Mato Grosso) and 201 (Rio Grande do Norte) deaths per 1000 live births, with higher values referring to States in North and Northeast Brazil. The standardised CVDMRs by place of birth (pob) were higher than those for place of residence (res), except in Santa Catarina State, whose values were the same. The CVDMR pob varied between 19.3 and 54.3 and the CVDMR res between 13.8 and 48.4 deaths per 10,000 inhabitants. When analysing the various regions of Brazil, a pattern was noted opposite to that found for the IMR: higher values for the CVDMR pob and res were observed for the South, Southeast and Centre-West regions.

The scatter for the Brazilian states relating IMR and CVDMR pob suggests an inverse relationship ($r = -0.45$). Two groups of States were noted with different scatter patterns: states in the North and Northeast regions presented higher values for the IMR and lower values for the CVDMR pob while states in the Southeast, South and Centre-West regions presented lower values for the IMR and higher for the CVDMR pob (Fig. 1). When the two groups of states are analysed separately (Fig. 2 Graphs 2a and 2b) the relationship between IMR and CVDMR pob appears as positive ($r = 0.21$ and $r = 0.46$, respectively for the states in the North and Northeast and the South, Southeast and Centre-West). Similar scatter patterns by IMR and CVDMR res are repeated for all the states ($r = -0.61$), and for those in the North and Northeast ($r = 0.33$) and South, Southeast and Centre-West ($r = 0.29$) regions.

The States of Paraíba and Rio Grande do Norte presented the highest values for IMR without the corresponding high values for CVDMR by pob and res. With the withdrawal of these atypical states, from the analysis concerning the North and Northeast regions, the correlation between IMR and CVDMR became even stronger ($r = 0.73$ and $r = 0.91$, respectively by pob and res).

Discussion

The estimated IMRs in the 1935 birth cohort were high, with a heterogeneous pattern amongst the Brazilian States, close to values found in Finmark, Norway, two decades earlier (Forsdahl, 2002) and exceeding those of England and Wales (40 to 120 per 1000 live births) in 1921–1925 (Barker, 1998). Due to the magnitude of the Brazilian IMRs, the use of the IMR as a proxy for low birth weight (intra-uterine malnutrition marker) as adopted in the studies on foetal programming (Barker, 1998) was appropriate in our study. However, it must be stressed that it is quite probable that many of the live births in 1935 with low birth weight died during the first year of life or before reaching adulthood (survival bias).

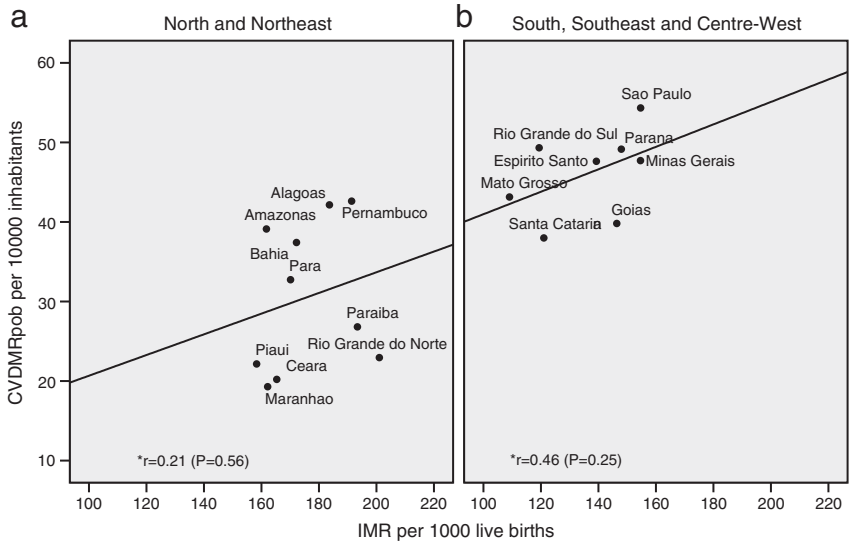

Fig. 2. Mortality rate distribution by cardiovascular disease at age 45–69 standardised by place of birth (CVDMRpob) and infant mortality rates (IMR) in 1935 Brazilian birth cohort by groups of regions: Graphic 2a: States in North and Northeast regions and Graphic 2b: States in South, Southeast and Centre-West regions.

The distributions of the standardised CVDMRs among Brazilian States by pob and res were similar, although the magnitude of the rates was always higher by pob. Exposure to intra-uterine malnutrition programmes for the baby for the appearance of chronic-degenerative diseases in adult life, will accompany the individual anywhere the person may live in the course of a lifetime, so that analyses based on CVDMR pob seem more appropriate to us.

In addition to waves of migration, the age distribution of the population may compromise the internal validity and interfere in the association investigated in our study. The analysis of the standardised CVDMR is intended to control, or at least mitigate such interferences. The reconstitution of CVDMR by age in the 1935 birth cohort, from a longitudinal standpoint, eliminated a possible cohort effect.

Our findings suggest a positive association between IMR and CVDMR in adult life in the 1935 birth cohort, when analysed by group of regions in Brazil. These regions are strongly related to varying socio-economic levels, register coverage and quality of mortality data, with the North and Northeast regions being the worst, the Centre-West being fair and the Southeast and South the best. Thus, the analysis stratified by groups of regions may help control the influences of regional variations.

The socio-economic conditions at the time of birth and early childhood, as well as in adult life are potential confounders for the association between low birth weight and mortality due to chronic-degenerative disease in adult life, as observed in ecological as well as in cohort studies (Fagerudd et al., 2004; Gillman, 2002; Lamont et al., 2000). Such association is not spurious, but weakens mainly when controlled by socio-economic conditions (Huxley et al., 2002).

Conclusions

There is a positive, although weak, association between IMR and CVDMR after controlling for migratory movements, cohort effects and socio-economic levels in the Brazilian 1935 birth cohort.

In order to prevent chronic diseases in future generations it's necessary to refocus attention on maternal nutrition and foetal growth (Barker, 1998). Besides this, epidemiological studies are needed to better understand the extent to which the effects of foetal programming are reversible, or may be modified later on.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

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