Infant mortality due to congenital malformation in Argentina (1998–2009): temporal and spatial analysis of neonatal and postneonatal components

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Introduction

The World Health Assembly (WHO 2010) approved a resolution that called on member states to “*prevent birth defects wherever possible, to implement screening programs, and to provide ongoing support and care to children with birth defects and their families.*” A resolution was adopted to help redress the limited focus to date on preventing and managing birth defects, especially in low- and middle-income countries.

As etiologies differ, infant mortality (IM) was decomposed into two components, the neonatal one covering the first 28 days of life and the postneonatal component comprising the remainder of the first year of life. The neonatal component is preferentially associated with endogenous causes (premature birth, birth sequels, or genetic disorders, among others), and the postneonatal component is concomitant with exogenous factors (infectious diseases, diarrhea, etc.) (Celton and Ribotta 2004).

In Argentina, there has been, in recent decades, a significant decrease in IM and its neonatal and postneonatal components associated with a change in the pattern of

causes of death, with an increase in those caused by congenital malformations (CM) (WHO 1998). Particularly, the recent pattern (2002–2006) of IM by CM in Argentina is characterized by a decrease in the rate of IM by CM (RIMCM) and concomitant increase in the percentage of deaths from CM (DCM%) (Bronberg et al. 2009). This pattern is similar to that observed in developed countries (Rosano et al. 2000). However, although the spatial distribution is practically uniform RIMCM, especially at the regional and provincial levels, the DCM% displayed wide geographical variation indicative of socio-economic, educational, and cultural interprovincial and interregional inequalities (Bronberg et al. 2012).

Previous studies indicate that, between 2002 and 2006 in Argentina, there were variations of the magnitude and trends of the early and late neonatal and postneonatal RIMCM and DCM% components. In the 5-year period under review, there was a steady decline in early neonatal RIMCM while late neonatal and postneonatal remained constant. Higher values of RIMCM occurred in the early neonatal period, followed by the late neonatal and postneonatal. DCM% values in the three components exceeded 20 % with a tendency to progressive involvement of CM in the causes of death (Bronberg et al. 2009).

In this study, we found that approximately 1.18/1,000 newborns die from cardiovascular system malformations, and these defects, along with those of the central nervous system, constitute 50 % of all child CM deaths, representing 35.6 % and 14.7 %, respectively (Bronberg et al. 2009). Next in order of magnitude are musculoskeletal system (8.6 %), chromosomal (5.8 %), digestive system (4.5 %), respiratory system (3.0 %), and genitourinary system (2.9 %) malformations (Bronberg et al. 2009).

Since knowledge of the temporal and spatial behaviors of neonatal and postneonatal IM by CM in Argentina is still

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inadequate, this paper proposes a deeper analysis of the secular trend and geographical differences of these components using the RIMCM and DCM%.

Subjects and methods

It is a descriptive eco-epidemiological study that gathered population information from databases of births and infant deaths occurred in Argentina. The data provided by the Bureau of Health Statistics and Information, Ministry of Health, came from live birth certificates and death certificates of children under 1 year of age for the period 1998–2009.

The following variables covering the period 1998–2009 were used: (a) absolute number of deaths, (b) absolute

number of live births, (c) CM deaths identified with ICD Tenth Revision Codes Q00–Q99 (PAHO 1995).

Based on these data, regardless of gender, RIMCM (number of infants dead with birth defects/1,000 live births) and DCM% (number of infants dead with birth defects/100 deaths) were calculated for the whole country and five geographical regions (Northwestern Argentina (NOA), Northeastern Argentina (NEA), Center, Cuyo, and Patagonia), Autonomous City of Buenos Aires (CABA) neonatal (0–28 days) component, and postneonatal (1 month to 1 year) component. The geographic regions were integrated as follows according to the National Institute of Statistics and Census: (a) center: Buenos Aires, CABA, Santa Fe, Córdoba, Entre Ríos, and La Pampa; (b) Patagonia: Neuquén, Chubut, Rio Negro, Santa Cruz, and Tierra del Fuego; (c) NOA: Catamarca, Tucumán, Salta, and Jujuy.

Fig. 1 Map of the regions and provinces of Argentina according to the National Institute of Statistics and Census (INDEC). *NOA*: Northwestern Argentina; *NEA*: Northeastern Argentina; *CABA*: Autonomous City of Buenos Aires

Table 1 Live births, deaths from congenital malformations (CM), rate of infant mortality due to congenital malformation (RIMCM), and percentage of death due to congenital malformation (DCM%) of the neonatal and postneonatal periods

Year	Live births	Deaths CM neo	Deaths CM post	RIMCM neo	RIMCM post	RMIMC neo/post ^a	DCM% neo	DCM% post	DCM% neo/post ^b
1998	683,301	1,583	905	2.32	1.32	1.58	19.87	17.96	1.11
1999	686,748	1,606	840	2.34	1.22	1.81	20.64	19.55	1.05
2000	701,878	1,645	821	2.34	1.17	1.93	21.50	20.69	1.04
2001	683,495	1,615	848	2.36	1.24	1.89	22.23	22.07	1.00
2002	694,684	1,708	771	2.46	1.11	2.02	21.82	19.91	1.10
2003	697,952	1,599	824	2.29	1.18	1.77	21.77	19.86	1.10
2004	736,261	1,656	754	2.25	1.02	2.11	23.09	22.16	1.04
2005	712,220	1,460	746	2.05	1.05	1.97	23.15	23.31	1.00
2006	696,451	1,497	756	2.15	1.09	1.91	25.36	24.52	1.03
2007	700,792	1,428	668	2.04	0.95	1.79	23.94	20.02	1.20
2008	746,460	1,531	754	2.05	1.01	1.97	24.71	23.97	1.03
2009	745,336	1,532	725	2.06	0.97	1.94	25.72	23.62	1.10
1998–2009	8,485,578	18,860	1,583	2.23	1.11	1.89	22.82	21.47	1.07

^a Rate of neonatal and postneonatal component due to RIMCM^b Rate of neonatal and postneonatal component due to DCM%

Jujuy, Santiago del Estero; (d) Cuyo: La Rioja, San Luis, San Juan, and Mendoza; and (e) NEA: Chaco, Corrientes, Formosa, and Misiones (Fig. 1).

The geographic regions were defined according to economic criteria used by the Federal Council of Investments (CFI 1963). Using census socioeconomic dimensions (education, health, and housing) and environmental conditions and attraction of the landscape, the welfare level of the population and its variation Argentina between 1991 and 2001 were analyzed by Velazquez (2010). In both decades, there were very noticeable differences between the Northwest and Northeast regions, historically the most neglected areas of the country; in relation to Patagonia and Central regions, the Cuyo region would be at an intermediate level (Velasquez 2010).

The secular trend for the entire period and interregional variation in risk for the periods 1998/2001, 2002/2005, and 2006/2009 were calculated using a Poisson regression model.

Spatial analysis was performed by searching for significant clustering of TIMCM at the department level and neonatal and postneonatal DCM% using SatScan software (Kulldorff et al. 2009).

Result

Between 1998 and 2009, 18,860 CM children died in the country in the neonatal period and 9,412 in the postneonatal

Fig. 2 Secular trend of rate of infant mortality due to congenital malformation (RIMCM) (a) and percentage of deaths due to congenital malformation (DCM%) (b) of neonatal and postneonatal components

period (Table 1). The decline in neonatal RIMCM for the whole period were 1.6 % and 2.6 % for postneonatal RIMCM. The DCM% increased by 2 % in the neonatal and postneonatal periods (Fig. 2).

The secular trend of neonatal and postneonatal RIMCM in the country throughout the period was significantly negative, more markedly in the postneonatal component (−0.026) than in the neonatal (−0.016) one (Fig. 2, Table 2). At the regional level, only NOA and Central regions had secular behavior similar to that observed in the country. In the NEA, Cuyo, and CABA, behavior was more heterogeneous (Table 2). Considering the period 2006–2009 throughout the country, a significant reduction of neonatal and postneonatal RIMCM of 12 % and 19 %, respectively (Table 3), was observed as compared with the 1998–2001 period. Northwestern and Central regions showed similar behavior to that of the country as a whole. The highest

significant reduction in the risk of neonatal RIMCM was observed in Cuyo, followed by the NOA, Center, and NEA.

The secular trend of neonatal and postneonatal DCM% in the country for the entire period was significantly positive (Fig. 2, Table 2); virtually no differences were observed between neonatal (0.021) and postneonatal components (0.020). A regional trend for both DCM% components presented a behavior similar to that observed for the country in all regions except Center and CABA, where, although the trend was also positive, it was not significant for both neonatal and postneonatal components (Table 2). Excluding CABA and Center for both neonatal and postneonatal components of DCM%, the highest positive secular trend was observed in Patagonia, followed by NEA, NOA, and Cuyo (Table 2). Considering the period 2006–2009 compared with the 1998–2001 period, increased neonatal and postneonatal DCM% of 18.5 % and 15.4 %, respectively, was observed

Table 2 Secular trend (ST), rate of infant mortality due to congenital malformation (RIMCM) and percentage of death due to congenital malformation (DCM%) of neonatal and postneonatal components

Rate of infant mortality due to congenital malformation	RIMCM							
	Neonatal				Postneonatal			
	1998–2001	2002–2005	2006–2009	ST	1998–2001	2002–2005	2006–2009	ST
Country	2.34	2.26	2.07	−0.016*	1.24	1.09	1.00	−0.026*
NOA ^a	2.11	2.11	1.89	−0.021*	1.07	1.04	1.02	−0.019*
NEA ^b	2.26	2.32	2.13	−0.014*	1.32	1.31	1.36	0.001 ns
Center	2.31	2.28	2.21	−0.016*	1.29	1.11	1.03	−0.037*
Cuyo	2.91	2.72	2.41	−0.019*	1.34	1.30	1.22	−0.016 ns
Patagonia	1.91	2.13	1.92	−0.006 ns	0.96	0.77	0.77	−0.019 ns
CABA ^c	1.99	1.76	1.78	−0.016 ns	0.90	0.86	0.73	−0.029*
Percentage of death due to congenital malformation	DCM%							
	Neonatal				Postneonatal			
	1998–2001	2002–2005	2006–2009	ST	1998–2001	2002–2005	2006–2009	ST
Country	21.06	22.46	24.93	0.021*	20.07	21.31	23.03	0.020*
NOA ^a	16.87	17.87	20.15	0.022*	15.11	18.55	21.50	0.037*
NEA ^b	14.21	15.37	17.84	0.028*	15.39	18.60	22.15	0.046*
Center	22.15	24.18	27.00	0.015*	24.79	25.60	26.47	0.005 ns
Cuyo	24.47	26.11	27.90	0.020*	23.57	26.60	31.96	0.031*
Patagonia	21.14	26.50	28.95	0.042*	19.37	21.41	26.80	0.051*
CABA ^c	27.63	29.13	32.90	0.020 ns	26.60	26.59	26.11	0.002 ns

ns not significant

^aNorthwestern Argentina

^bNortheastern Argentina

^cAutonomous City of Buenos Aires

* $p < 0.05$, significant level

for the whole country (Table 3). The regional risk reduction of DCM% was zero for the postneonatal component in the Center and CABA. Regionally, excluding Center and CABA, the variation in DCM% risk presented virtually the same pattern for both components, while the highest decrease was observed in the NEA and Patagonia (Table 3).

Figure 3 would indicate that certain components of the neonatal and postneonatal RIMCM clusters with higher rates and greater risk, significantly different from the whole country figures, would be located in the north of Argentina. The opposite would be observed with respect to the components in DCM%, whose clusters of high percentages, significantly different from the country's, were located in the central part of Argentina (Fig. 4). Only the neonatal component of DCM%

presented low percentage clusters located in the northern part of Argentina (Fig. 4).

Discussion and conclusions

This paper analyzes the trend of IM neonatal and postneonatal components by CM in Argentina using two indicators: the rate and percentage of deaths by CM. Both indicators provide complementary information on the risk of infant death by CM, comparable over time and across countries, regions, provinces, etc., and also represent a useful measure of the burden of child deaths by CM of interest to public health, the formulation of health policies, and an understanding of the scope of CM as a risk factor of

Table 3 Risk and reduction (%) of rate of infant mortality due to congenital malformation (RIMCM) and risk and increase (%) of percentage of death due to congenital malformation (DCM%) in the sub-period 2002–2005 and 2006–2009 in relation to sub-period 1998–2001

Risk and reduction (%) of rate of infant mortality due to congenital malformation	RIMCM							
	Neonatal				Postneonatal			
	2002–2005		2006–2009		2002–2005		2006–2009	
	Risk	Reduction (%)	Risk	Reduction (%)	Risk	Reduction (%)	Risk	Reduction (%)
Country	0.96*	–3.5	0.88*	–11.5	0.88*	–12.1	0.81*	–19.0
NOA ^a	0.95 ns	–4.6	0.85*	–14.6	0.93 ns	–7.5	0.85*	–14.9
NEA ^b	0.97 ns	–2.3	0.89*	–11.0	0.99 ns	–0.1	1.02 ns	0.0
Center	0.95*	–4.8	0.88*	–11.8	0.82*	–17.6	0.75*	–25.4
Cuyo	0.94 ns	–5.9	0.84*	–15.8	1.00 ns	0.0	0.89 ns	–10.9
Patagonia	1.00 ns	0.0	0.96 ns	–4.2	0.78*	–22.2	0.83 ns	–17.2
CABA ^c	0.89 ns	–11.3	0.90 ns	–9.9	0.96 ns	–4.1	0.81 ns	–18.6
Risk and increase (%) of percentage of death due to congenital malformation	DMC%							
	Neonatal				Postneonatal			
	2002–2005		2006–2009		2002–2005		2006–2009	
	Risk	Increase (%)	Risk	Increase (%)	Risk	Increase (%)	Risk	Increase (%)
Country	1.06*	6.6	1.18*	18.5	1.06*	6.1	1.15*	15.4
NOA ^a	1.03 ns	2.9	1.22*	22.3	1.17*	17.2	1.33*	32.9
NEA ^b	1.05 ns	5.3	1.24*	23.7	1.22*	21.8	1.44*	44.1
Center	1.06*	6.3	1.13 ns	12.7	0.98 ns	0.0	1.01 ns	0.0
Cuyo	1.08 ns	7.7	1.15*	15.0	1.16 ns	16.3	1.29*	28.7
Patagonia	1.20*	20.4	1.36*	35.9	1.06 ns	6.5	1.42*	41.9
CABA ^c	1.06 ns	5.9	1.19*	19.5	1.01 ns	1.1	0.99 ns	0.0

ns not significant

^aNorthwestern Argentina

^bNortheastern Argentina

^cAutonomous City of Buenos Aires

* $p < 0.05$, significant level

infant deaths (Penchszadeh 1993; Copeland and Kirby, 2007).

While the validity of death certificates as a source of information for epidemiological analysis of deaths has been questioned due to underreporting of CM (Copeland et al. 2007; Northam and Knapp 2006; Rosano et al. 2000) on account of deficiencies in the capability and quality of diagnosis (description, classification, and coding), this is the only population-level information collected from multiple countries which, supported or promoted by international agencies such as WHO (1998), is useful for comparative purposes. However, the validity of these certificates has been confirmed for the identification of neural tube defects (Tairou et al. 2006).

According to PAHO in Argentina, the percentage of poorly defined or unknown causes (2007) is 7.5 and the overall underreporting of mortality, 4.8 (2005–2007), compared with 10.9 and 23.5, respectively, of South America (PAHO 2009).

There is no similar information for Argentina at the regional level. The close relationship between overall IM and other socio-economic indicators, especially in the poorest regions of the north, would indicate a constant rate

of underreporting across the country which would exclude biasing in interregional comparison. Moreover, the rate of underreporting in South America experienced a decrease of 21.8 % (2007–2009) (PAHO 2007, 2009) probably due to strong policies implemented by hospital committees on analysis, study, and research of infant deaths.

The growing recognition that reducing IM cannot be achieved without a substantial reduction in neonatal deaths has increased interest in preventing these deaths (Rowley and Hogan 2012; Rowley et al. 2012). Between 1990 and 2009, the overall rate of neonatal IM declined by 28 % from 33.2 to 23.9 deaths per 1,000 live births. In the Americas, this decline was almost double (48.3 %) (Oestergaard et al. 2011). In 2010, 270,000 malformed children in the world died in the neonatal period; these deaths represented about 4 % of all deaths in children under 5 years of age (Liu et al. 2012). No reliable data are available globally on the incidence of deaths from CM in the postneonatal period, but, between 1989 and 2002 in the United States, CM accounted for 79 % of all child deaths in this period (Yang et al. 2006).

The behavior of neonatal and postneonatal components of DCM% and RIMCM in Argentina was similar for the

Fig. 3 Clusters of low and high risk of RIMCM of neonatal and postneonatal components at department level

total IM (neonatal+postneonatal) to that observed by Bronberg et al. between 2002 and 2006: While the RIMCM decreased, the DCM% increased. This behavior has been attributed to the change in child morbidity pattern determined by the rapid decline globally and in the Americas, particularly in Argentina, Chile, and Uruguay, of child deaths from pneumonia and diarrhea (Celton and Ribotta 2004; Rajaratnam et al. 2010; Liu et al. 2012; Bronberg et al. 2012). The same trend in both indicators in the neonatal and postneonatal periods, decreased RIMCM and increased DCM%, were observed at the regional level but with different levels of significance (Tables 1 and 2).

The decline in neonatal and postneonatal components of RIMCM in Argentina was also similar to that observed for the same components of the overall IM from 1950–2000 (Celton and Ribotta 2004). In this period, according to Celton and Ribotta (2004), the decline in total neonatal and postneonatal IM was 58.1 % and 86.5 %. Data temporarily closer to period analyzed in this paper indicated that, between 1990 and 2010 in Argentina, the neonatal and postneonatal IM came down by 47 % and 64 %, respectively (Rajaratnam et al. 2010). The magnitude relationship between total neonatal and postneonatal mortality was similar to that observed in this

work for neonatal (11 %) and postnatal (27 %) RIMCM, all of which indicated that the largest reduction of IM by CM in Argentina, MI as the total, was mainly due to the decrease in postneonatal component, which experienced a significant reduction for the whole country of 19 % compared with the 12 % neonatal component between 2006 and 2009 (Table 3). The differences in the decline between neonatal and postneonatal RIMCM probably obeyed to greater control of reducible and preventable causes of child deaths associated with CM in the postneonatal period.

However, both RIMCM components had regional disparities as, between regions with a statistically significant positive secular trend of neonatal RIMCM, only NOA and Cuyo showed a greater decrease than national results in the 2006–2009 sub-period (Table 3). Regarding the postneonatal component of RIMCM, the sharpest decline of 25 % was observed in the Central region. It is noteworthy that, in the CABA, although a secular trend was observed for both RIMCM components, risk reduction was lower than the national trend and not statistically significant in the two sub-periods (Table 3), so these results would indicate a stagnation of the secular change of the IM for CM and its components. The observed variations in RIMCM behavior between regions would obey differential

Fig. 4 Clusters of low and high risk of DCM% of neonatal and postneonatal components at department level

interaction of the following dimensions: (a) health and welfare of the population at the beginning of the review period, (b) socioeconomic and demographic characteristics of the population, (c) effective implementation of measures and policies implemented to reduce IM, (d) structures, capabilities, and resources to prevent or reduce newborn deaths (Fariña et al. 2010). In relation to this hypothesis, Fig. 3 shows that precisely the departments with higher and statistically significant neonatal and postneonatal RIMCM, compared with the rest of the country, would be located in the most impoverished and least developed regions of the country.

As for the DCM%, it showed a similar secular trend in both components (Table 1), with a percentage increase between the beginning and the end of the reporting period slightly higher in the postneonatal component (31.5 %) compared with the neonatal component (29.4 %). However, it can be noted that the increase in neonatal DCM% was higher than postneonatal DCM% in the last phase (2006–2009) of the period under study (Table 3), indicating the participation percentage increased and accelerated the CM as a cause of newborn deaths in the neonatal period. This indicator is sensitive to the socioeconomic conditions of the population. According to Rosano et al., the DCM% is positively related to the GDP, and Argentina showed the same relation to the socio-economic development and quality of life achieved by the population. The higher the development and human welfare the higher the DCM% of the population (Bronberg et al. 2012). This was evidenced by the regional heterogeneity of the behavior of this indicator with the highest percentages in relation to the country, in the neonatal and postneonatal components in wealthier areas of the country (Table 3, Fig. 4) (Velazquez 2010).

The spatial behavior of neonatal and postneonatal RIMCM and DCM% in relation to the socio-economic conditions of the country as shown in Figs. 3 and 4 is similar in general to that observed without decomposing them. Bronberg et al. (2012) analyzed the correlation of the total DCM and RIMCM% (neonatal–postneonatal) at the departmental level with longitude and latitude and a socioeconomic indicator, comprising 21 variables of the 2001 Census of Population and Housing. The RIMCM was not significantly associated with the country's patent socioeconomic heterogeneity; the highest values of DCM%, however, were observed in populations of central and southern regions of the country. The socioeconomic indicator explains 41 % of the variation in DCM%.

The proportion of newborn deaths attributed to each cause varies according to the development of each country or region. In those places where the neonatal IM is lower, prematurity and birth defects play a more important role. In countries with high rates of neonatal IM, contributions from other causes (asphyxia, tetanus, and infections) are higher (Fariña et al. 2010). There is a globally growing trend in the reduction of neonatal IM, regardless of the socio-economic status of each

country (Rajaratnam et al. 2010; Liu et al. 2012). However, the magnitude of the reduction of the specific causes of neonatal deaths and their trend differ from each other. Generally, those attributable to CM vary less than the others. Between 2000 and 2010, the global annual rate of change of neonatal IM by CM was -0.7% , lower than that of pneumonia (-2.2%), diarrhea (-4.0%), preterm birth complications (-2.0%), and related to childbirth causes (-2.4%). In the Americas, the decline in newborn deaths by CM was higher, at -1.3% , but even more important was the reduction of deaths from pneumonia (-6.3%) and diarrhea (-12.3%).

In developing countries, a condition that characterizes Argentina and especially the poorest regions in the north, the main effort and health policies of the last 50 years have been aimed at controlling the exogenous causes of IM. Only in recent years, endogenous causes and with them the CM have started to be regarded as a specific health problem that requires major specific changes for which the health system has not yet been sufficiently trained and/or policies recently implemented since 2003 have been insufficient and/or partially exploited.

Local knowledge of the disparities regarding the specific causes of infant deaths in the neonatal and postneonatal periods would allow on the one hand to alert health authorities about these changes in the pattern of causes of infant deaths and the on other, to set priorities to ensure the survival of newborns affected by these conditions and the allocation of resources according to their severity and complexity. Indicators of IM by CM used in this work constitute appropriate tools to achieve this knowledge and set these policies.

In Argentina, RIMCM reduction could be given by (a) improved diagnosis and reporting of cases, (b) consequences of the health transition on patterns of morbidity with more control of the causes of death from infections and malnutrition and its gradual replacement by the CM, (c) quality improvement and availability of medical and surgical care, (d) effectiveness of a policy of primary prevention, such as folic acid fortification and control of rubella vaccination, and (e) implementing the Congenital Heart Disease Program (Chernovesky 2011) and the National Registry of Congenital Anomalies (Groisman et al. 2012). Particularly in Argentina, after the implementation of Law No. 25630 of mandatory fortification of wheat flour with folic acid in 2003, the mortality risk for anencephaly was significantly reduced by 53 % for the whole country with substantial regional disparities observed (Bronberg et al. 2011).

It was concluded that the IM components by CM analyzed with RIMCM and DCM% have a behavior similar to IM by total MC, characterized by a RIMCM decrease and a DCM% increase, more marked in the postneonatal component, with spatial differences regarding variations of such indicators very likely related to socioeconomic inequality in the country.

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