Original

Infant mortality due to congenital defects in Costa Rica: 2010-2018 update.

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Abbreviations:
CD, congenital defect; INEC, Instituto Nacional de Estadística y Censo de Costa Rica; IMR, infant mortality rate; IMBD, infant mortality rate due to congenital defects; NMR, neonatal mortality rate; NDMR, the neonatal mortality rate due to congenital defects; PR, prevalence ratio.
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Abstract

Aim. This study aims to identify the trend of the different types of congenital defects in the infant and neonatal mortality rate in Costa Rica during the period 2010-2018 and to compare it with the period 2000-2009.

Methods. A vital statistics analysis was performed. The source of information was the Costa Rican National Institute of Statistics and Censuses, through its public domain system and online consultation, the base of deaths by cause and the base of births for the period 2000-2018 were consulted. The causes of death due to congenital defects were grouped by system, in addition, the defects with the highest mortality in the study period were selected for their specific analysis. To describe the behavior of infant mortality due to congenital defects in 2010-2018 concerning the previous decade, infant and neonatal mortality rates were calculated for the periods 2000-2009 and 2010-2018 with their respective confidence interval (95% CI). A linear Poisson Log regression model was constructed for each group of congenital defects and for the specific defects selected, taking the sub-periods compared as an adjustment factor. Prevalence ratios were estimated and compared using Wald's chi-square based on the period 2000-2009.

Results. In the last two decades, birth defects caused 29% to 38% of overall infant mortality. The infant mortality rate due to congenital defects from 2000 to 2009 was 3.19 (95% CI: 3.06-3.32) and presented a significant decrease to 2.97 (95% CI: 2.84-3.11) in the 2010-2018 period. This decrease was given at the expense of the impairment of the circulatory and digestive systems. When analyzing infant mortality due to specific congenital defects, a significant decrease was shown only in spina bifida and some cardiac defects: transposition of the great arteries, ventricular septal defect, aortic coarctation, and other unspecified cardiac anomalies. The neonatal mortality rate due to congenital defects did not vary significantly between the periods compared, in 2000-2009 it was 2.13 (95% CI: 2.03-2.24) and 2.17 (95% CI: 2.06-2, 29) in 2010-2018. The only group of congenital defects that presented a significant decrease in the neonatal mortality rate in the last decade was the circulatory system.

Conclusions. In the last decade, there was a significant decrease in the infant mortality rate due to congenital defects. This decrease was mainly due to a significant decrease in infant and neonatal mortality rates from heart defects.

Keywords: Infant mortality, neonatal mortality, birth defects, Costa Rica.

About 3% to 5% of all newborns worldwide are born with a birth defect (CD).[1] Its n with serious CD and 95% of deaths, largely due to high birth rates and limited access to prenatal diagnosis. [2]

In the 1980s, in Latin America and the Caribbean, the proportion of infant deaths attributed to CD increased from 2% to 27% and, since then, they represent one of the 5 leading causes of death in the region (Health conditions in the Americas. Pan American Health Organization, 1986). In Latin American countries, where infant mortality has fallen below 50 per 1 000 births, the CD is the third leading cause of death, which makes it a significant public health problem.[3]

In the last decade, Costa Rica, a middle-income country, presented an annual average of 71 000 births (98% in-hospital) and an infant mortality rate (IMR) of 8.37 for the year 2018; CD accounted for 35% of the IMR, surpassed only by perinatal conditions (Annual bulletin. Instituto Nacional de Estadística y Censos Infant mortality and recent evolution 2018). The prevalence of CD in the last five years in Costa Rica ranged between 2.6-3.2 per 100 births (Annual birth defects report. Inciensa, 2019).

The IMR is an indicator of the living conditions and environment in which a nation develops. It is one of the best and most accessible indicators of the health of a population, synthesizing many of the components of health while being sensitive to both health interventions and general living conditions.[4]

The most marked reduction in the IMR in Costa Rica occurred in the 1970s and 1980s, mainly due to the decrease in infectious, immunopreventable, and parasitic diseases (Desigualdades de Salud en Costa Rica: Una aproximación geográfica – poblacional / Health Inequalities in Costa Rica: a geographic-population approach. PAHO, 2004). This phenomenon had a multifactorial origin, since it occurred in a context of great economic and social improvements, a notable drop in fertility, and a radical transformation of health programs and organization of the sector.[5]

While there are many studies analyzing infant mortality and its risk factors, the contribution of CD to IMR and neonatal mortality rate (NMR) has been much less explored.

The last analysis of the IMR for birth defects (IMBD) in Costa Rica has carried out with data from 1981 to 2010.[6] This report identified a significant reduction in IMR in the nervous, digestive and circulatory system CD groups; except for the circulatory system, these groups experienced a significant drop in their NMR. However, an analysis of specific congenital defects was not performed, but only by the system, leaving the question as to which specific DC has the greatest weight in the IMBD.

In the last decade, events related to CD have occurred that could have affected IMBD. One of them has been the management adopted since 2014 by the Hospital Nacional de Niños as a national reference center for diagnosis and cardiac surgery in children, to improve surgical interventions in children with congenital heart disease (Caja Costarricense de Seguro Social, 2016. https://www.ccss.sa.cr/noticia?logros-espectaculares-en-cirugia-cardiaca-pediatrica). Another event was the zika virus emergency in the country in 2016, with a corresponding increase in some central nervous system defects, such as microcephaly (Abbreviated report of microcephaly cases reported to CREC, Costa Rica, 2011-2017). In this context, South American countries such as Brazil, demonstrated a 5% increase in IMR in 2016 compared to 2015, attributed according to health authorities to the zika virus epidemic and the economic crisis.[7]

This study aimed to identify the trend of the different types of congenital defects in IMT and NTM in Costa Rica from the period 2010 to 2018 and to perform a comparative analysis with the period 2000 to 2009.

Methods

An analysis of vital statistics was conducted. The source of information was the Instituto Nacional de Estadísticas y Censos de Costa Rica (INEC) through its online consultation system (https://www.inec.cr/sistema-de-consultas) for demographic statistics with public access. The base of deaths by specific cause and the base of births for the period 2010-2018 was consulted. In addition, although both the IMRBD and the neonatal mortality rate due to congenital defects (NDMR) had already been analyzed in a publication,[6] the same databases were consulted to obtain the estimates for the period 2000-2009, to compare them with the new period to be analyzed 2010-2018 and adjust the trend according to period, for congenital anomalies

in general and by specific CD. This last analysis was not done in the previously mentioned report, as it provided estimates only by large groups of CD. Details of the causes by CD of neonatal deaths were obtained from the tables prepared for this purpose by INEC each year[1] , which are classified according to the Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death in its tenth edition.

The IMBD and IMBD rates year were calculated, as well as their trend in the period 2000-2018. In addition, the weight of infant and neonatal deaths due to CD in the overall IMR was calculated.

The following groups of congenital defects were analyzed: nervous system (Q000-Q079), circulatory system (Q200-Q289), respiratory system (Q300-Q349), digestive system (Q380-Q459), urinary system (Q600-Q649), musculoskeletal system (Q650-Q799), other syndromes and congenital anomalies (Q860-Q899), chromosomal anomalies (Q900-Q999) and finally skin, face, neck, and genital DC were grouped (Q800-Q859, Q100-Q189, Q350-Q379, Q500-Q564).

The main specific causes of infant and neonatal death by CD were identified and the defects with the highest number of deaths during the 19 years of analysis were selected.

For trend analysis, a linear Poisson Log regression model was constructed (module: generalized linear models, software: SPSS. Statistics) adjusted by period, taking as a base the period 2000-2009, not only for each CD group but also for the main specific causes of infant mortality by CD. The model used is represented as follows:

Log (mortality rate) = β_0 + β_1 × (period of time)

From this model, marginal means were obtained for the IMBD and IMBD rates, as well as the prevalence ratios (PR) corresponding to the periods with their respective confidence intervals (95%CI). These results were compared using the Wald chi-square tests. The significance level used was 0.05.

The results were grouped in two tables and one figure. Table 2 shows the CDs with more than 50 deaths during the period analyzed.

[1]   Neonatal deaths by cause of death and sex.

This report corresponds to an analysis of publicly available vital statistics and was approved by the Research Directorate of the Costa Rican Institute for Research and Education in Nutrition and Health (INCIENSA).

Results

In Costa Rica, the trend of the overall IMR in the last 19 years (2000-2018) has been downward, ranging between 11.1 and 7.7 per 1,000 births. However, the NMR, which occupies about 71% of the IMR, has presented a much more discrete decline, ranging between 7.6 and 5.9 per 1000 births. CD accounted f or 33.6% of infant mortality during these almost two decades, while neonatal deaths due to CD accounted for 32% of total neonatal deaths. The NIDDMR ranged between 2.5 and 3.7 per 1000 births, showing a decrease; while the NIDDMR ranged between 1.8 and 2.4 per 1000 births, but its behavior was practically flat (Figure 1).
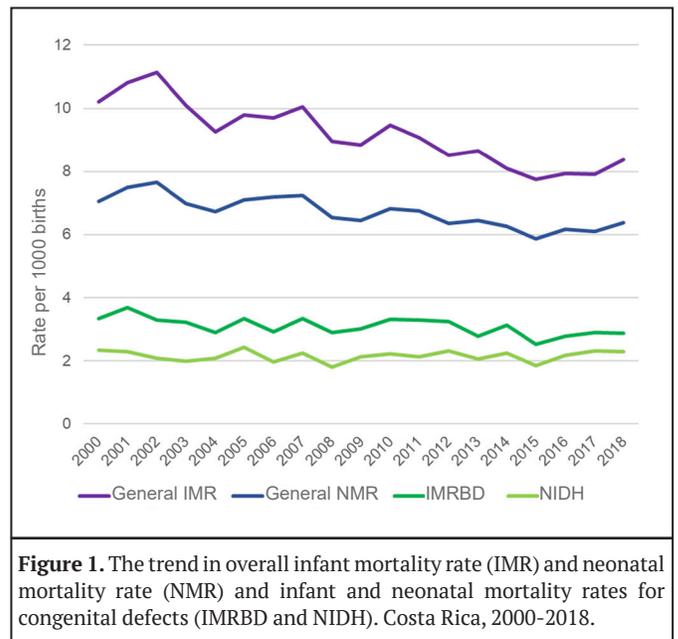

Figure 1. The trend in overall infant mortality rate (IMR) and neonatal mortality rate (NMR) and infant and neonatal mortality rates for congenital defects (IMRBD and NIDH). Costa Rica, 2000-2018.

To analyze the significance of these changes, a period-adjusted Poisson regression was performed, comparing the period 2010-2018 versus 2000-2009. In the 2010-2018 period, the overall IMR was 8.42 per thousand (95% CI: 8.2-8.65) and presented a significant decrease from the previous decade (9.88 per thousand, 95% CI: 9.7-10). The IMRDMR also presented a significant decrease of 7% in the period 2010-2018 (Table 1), going from 3.19 to 2.97 per

thousand; however, as the decrease in the overall IMR was greater than the decrease in the IMRDMR, the percentage contributed by CD in the IMR in the last decade is higher going from 32.25% in the period 2000-2009 to 35.43%. Concerning the overall NMR, there was also a significant decrease from 7.04 (95%CI 6.8-7.2) to 6.34 per thousand (95%CI 6.2-6.5); however, there was no significant change in the NCMR, which went from 2.13 to 2.17 per thousand, or in the percentage weight of CD in the NMR.

When analyzing the different CD groups separately, we see that the decrease in the IMBD was mainly at the expense of the circulatory and digestive systems. In all the other CD groups, the difference was not significant or there was even an increase, the latter being significant only in the respiratory system (Table 1).

About the NCMDD, an increase of 2% was observed in the periods analyzed, but this change was not statistically significant. Only the circulatory system, 99.8% of whose defects correspond to congenital heart disease, showed a significant decrease of 25%, while the other systems showed no significant changes or an increase, as was the case with the respiratory system and chromosomopathies (Table 1).

Table 1. Infant and neonatal mortality according to birth defects (CD) groups and prevalence ratio, for the period 2010-2018, based on the period 2000-2009.

DC System/Group	N (percentage)		Mortality rate per thousand births		Prevalence ratio	p
	2000-2009	2010-2018	2000-2009	2010-2018	(95%CI)	
Infant Mortality						
Circulatory	959 (40,8)	610 (32,1)	1,30	0,95	0,73 (0,66-0,81)	<0,05
Nervous	372 (15,8)	306 (16,1)	0,50	0,48	0,95 (0,81-1,10)	NS
Chromosomal abnormalities	239 (10,2)	236 (12,4)	0,32	0,37	1,14 (0,95-1,36)	NS
Osteomuscular	227 (9,7)	188 (9,9)	0,31	0,29	0,95 (0,79-1,16)	NS
Other syndromes/anomalies	194 (8,3)	198 (10,4)	0,26	0,31	1,18 (0,97-1,43)	NS
Respiratory	134 (5,7)	206 (10,8)	0,18	0,32	1,77 (1,43-2,20)	<0,05
Urinal	103 (4,4)	82 (4,3)	0,14	0,13	0,92 (0,69-1,23)	NS
Digestive	105 (4,5)	60 (3,2)	0,14	0,09	0,66 (0,48-0,91)	<0,05
Skin, genitals, face, neck	16 (0,7)	13 (0,7)	0,02	0,02	0,94 (0,45-1,95)	NS
Total (DC)	2349 (100)	1899 (100)	3,19	2,97	0,93 (0,88-0,99)	<0,05
Neonatal mortality						
Circulatory	543 (34,6)	353 (25,4)	0,74	0,55	0,75 (0,65-0,86)	<0,05
Nervous	254 (16,2)	233 (16,8)	0,34	0.36	1,06 (0,89-1,26)	NS
Chromosomal abnormalities	162 (10,3)	195 (14)	0,22	0,31	1,39 (1,13-1,71)	<0,05
Osteomuscular	206 (13,1)	166 (12)	0,28	0,26	0,93 (0,76-1,14)	NS
Other syndromes/ anomalies	166 (10,6)	175 (12,6)	0,23	0,27	1,22 (0,98-1,5)	NS
Respiratory	92 (5,9)	152 (10,9)	0,12	0,24	1,90 (1,47-2,47)	<0,05
Urinal	92 (5,9)	75 (5,4)	0,12	0,12	0,94 (0,69-1,27)	NS
Digestive	44 (2,8)	31 (2,2)	0,06	0,05	0,81 (0,51-1,29)	NS
Skin, genitals, face, neck	11 (0,7)	9 (0,6)	0,01	0,01	0,94 (0,39-2,28)	NS
Total (DC)	1570 (100)	1389 (100)	2,13	2,17	1,02 (0,95-1,10)	NS

Note: The average annual number of births for the periods 2000-2009 and 2010-2018 were 73 707 and 71 018 respectively. In total there were 737 074 births for the period 2000-2009 and 639 163 births for the period 2010-2018.

Table 2 shows the change in IMR according to specific CD; a significant decrease in causality was identified for some cardiac defects such as transposition of the great arteries, ventricular septal defect, coarctation of the aorta, and other unspecified cardiac anomalies. Some other DC that presented significant changes does not appear, because the number of deaths was less than 50 as the established limit. However, among the latter, spina bifida presented a significant decrease in IMR (p <0.05) from 2.58 to 1.10 per 100 thousand births (PR: 0.42; a decrease of 58%); while other CD presented a significant increase (p <0.01) in their IMR, such as gastroschisis that went from 1.36 to 4.69 x 100 thousand births (PR: 3.46; increase of 246%), Siamese twins from 0.41 to 2.82 x 100 thousand births (PR: 6.92; increase of 592%) and code Q870-8 corresponding to "other specified syndromes" whose IMR increased from 2.04 to 5.16 x 100 thousand births (PR: 2.54; an increase of 154%). Pulmonary hypoplasia and dysplasia also showed a significant increase (Table 2).

Table 2. Infant mortality rate due to congenital defect (IMRBD) and prevalence ratio, for the period 2010-2018, based on the period 2000-2009.

Congenital defect	Code	IMRBD x 100 thousand births		Prevalence ratio (95%CI)	p
		2000-2009	2010-2018		
Anencephaly	Q000	15,87	15,96	1,01 (0,77-1,31)	NS
Hydrocephalus	Q030-9	8,68	6,10	0,70 (0,47-1,05)	NS
Holoprosencephaly	Q042	4,61	4,85	1,05 (0,65-1,71)	NS
Hypoplasia of the encephalon	Q043	10,18	10,80	1,06 (0,76-1,47)	NS
Transposition of great arteries	Q203	8,55	3,75	0,44 (0,27-0,7)	<0,01
Ventricular septal defect	Q210	8,82	4,38	0,50 (0,32-0,77)	<0,01
Atrioventricular defect	Q212	6,78	5,32	0,78 (0,51-1,21)	NS
Tetralogy of Fallot	Q213	4,88	3,29	0,67 (0,39-1,15)	NS
Left heart hypoplasia	Q234	14,38	11,73	0,82 (0,61-1,1)	NS
Other Heart, unspecified	Q249	44,50	27,22	0,61 (0,51-0,74)	<0,01
Patent ductus arteriosus	Q250	3,66	4,69	1,28 (0,76-2,16)	NS
Coarctation of the Aorta	Q251	5,02	2,19	0,44 (0,24-0,81)	<0,01
Anomalous pulmonary vein connection	Q264	7,87	6,10	0,78 (0,52-1,16)	NS
Pulmonary hypoplasia and dysplasia	Q336	15,47	28,79	1,86 (1,47-2,35)	<0,01
Other malformations of the intestine	Q430-8	5,56	3,75	0,68 (0,41-1,12)	NS
Potter's syndrome	Q606	7,46	7,20	0,96 (0,65-1,43)	NS
Diaphragmatic hernia	Q790	18,04	14,39	0,80 (0,61-1,04)	NS
Multiple malformations	Q897	21,98	21,28	0,97 (0,77-1,22)	NS
Down Syndrome	Q909	7,46	8,45	1,13 (0,78-1,65)	NS
Edwards Syndrome	Q913	16,42	19,40	1,18 (0,92-1,52)	NS
Patau's syndrome	Q917	7,73	9,39	1,21 (0,84-1,74)	NS

Note: Defects with more than 50 deaths during the period analyzed are included.

Regarding the NMR by specific CD, a significant decrease (p<0.01) was identified in only two cardiac defects: transposition of the great arteries, which went from 5.16 to 2.35 per 100 000 (PR: 0.46; 54% decrease) and other unspecified cardiac anomalies, which went from 27.68 to 15.18 per 100 000 (PR: 0.55; 45% decrease). This last group (unspecified cardiac anomalies) corresponds to a series of congenital heart diseases that were not defined at the time of filling out the death certificate, either because they had not been diagnosed at the time of death registration or because the diagnosis was not correctly noted.

The same specific DCs that showed significant increases in IMR did so in NMR: gastroschisis which went from 1.22 to 3.75 x 100 thousand births (PR: 3.08; 208% increase), pulmonary hypoplasia and dysplasia which rose from 10.85 to 22.06 x 100 thousand births (PR: 2.03; 103% increase); Siamese twins, from 0.41 to 2.82 x 100 thousand births (PR: 6.92; 592% increase); and other specified syndromes, from 0.68 to 2.66 x 100 thousand births (PR: 3.92; 292% increase).

In general, the digestive system showed a significant decrease in infant mortality, but not in neonatal mortality. However, when disaggregating the main digestive anomalies as a cause of death, although there was a decrease in all of them, none of them was significant.

Discussion

By identifying the trend of the different types of birth defects in IMR and NTMR in the country during the period 2010-2018 and performing a comparative analysis with the period 2000-2009, it was found that, in Costa Rica, previous analyses showed a significant decrease in both IHMR and NSTEMI from 1981 to 2010.[6] With this work, a significant decrease in both IMR and NTMR was documented between 2010-2018 concerning the previous decade. Likewise, a significant decrease of 7% was documented in the IHMR, even though the NCMR did not show significant changes.

Around the world, despite advances in the reduction of IMR, the decrease in U5MR has not been as relevant.[8] Thus, CD constitutes one of the great challenges for health agendas worldwide and particularly in the Americas region, whereby in 2017, 15 out of every thousand births were at risk of dying during the first year of life and 10 out of every thousand during the first month (United Nations Inter-agency Group of Child Mortality Estimation. Levels and trends in child mortality: report 2018. United Nations Children's Fund, 2018).

In Latin America, approximately one in five neonatal deaths in the region is due to CD; moreover, the proportion of neonatal deaths due to CD has increased from 16.2% to 22.3% between 2000 and 2016, an increase that is notable in most countries worldwide.

A recent analysis by the Pan American Health Organization (Present and Future of Birth Defects Surveillance in the Americas. PAHO-World Bank, 2019) it was determined that in countries where the NIMR is less than 6 per 1000 births, CD deaths represent 15%-40% of the total; those with a NIMR between 6 to 12 per 1000 births, the percentage weight fluctuates between 10%-30%; while, for those countries where the NIMR is higher than 12 per 1000, CD deaths generally represent less than 15% of the total in that age group. Referring to the results of this analysis, in Costa Rica, where the NIMR is 6.34 per 1000, neonatal deaths due to CD accounted for 32% of overall neonatal mortality. Also, at the national level, the NCMR for the period studied represented 73% of the IDDMR; and it has been reported that, in developed countries, 70% of deaths due to congenital anomalies occur in the neonatal period.[9]

Contrary to what has happened in our country, some Latin American countries have shown an increase in the IMR in recent decades.[10,11] In Mexico, for example, the IMR decreased by more than 57% between 1990 and 2012; however, infant deaths due to CD remained stable, with a slight upward trend, so their relative weight increased from 13.7% to 33.8%.[12] In Brazil, during the period 1996-2010, there was an increase in both the U5MR and the percentage of deaths due to CD.[13]

On the other hand, similar to our country, in the United States, a country where CD occupies the first place as a cause of infant mortality,[14,15] the IMRBD has been decreasing since 1970, during the period 2003-2017 it decreased by 10% overall.[16] According to the authors, the decrease in the IMRBD could have been influenced by improvements in prenatal care, prevention measures, and improvements in medical care, in addition to factors influencing overall infant mortality.

In Costa Rica, congenital heart disease is the most frequent CD and is the leading cause of infant mortality due to CD.[17] According to our analysis, IMR and NMR for this cause decreased by 27 and 25% respectively from 2010 to 2018 compared to the previous decade. Thus, being a group of CD that is serious as well as frequent, a significant decrease in their mortality greatly impacts the IMRBD and NMRCD. This is what happened in our country; the decrease in the IMRBD was mainly due to a significant decrease in infant and neonatal mortality in cardiac

defects. This is the first time in our country that a significant decrease in neonatal mortality for these reasons is evidenced, a phenomenon that requires further analysis to find out which factors contribute to this important improvement.

With IMR and NMR for nervous system defects in general, there was no significant change between the periods analyzed, nor was there a change for CD associated with congenital Zika (microcephaly, hypoplasia of the encephalon, hydrocephalus). However, there was a significant decrease in infant mortality due to spina bifida, a fact already documented in the country and with the main decrease in IMR due to neural tube defects after 1997, mainly as a consequence of food fortification with folic acid.[18]

The only system that presented an increase in IMR was the respiratory system. However, it is important to clarify that 88% of the anomalies correspond to pulmonary hypoplasia and dysplasia (Q336), a possibly misclassified cause of death, which could be more related to a complication of prematurity than to a congenital defect. Similar results have been found in other analyses and suggest that this trend could be due to an increase in the misuse of this diagnosis.[19]

Chromosomal anomalies as a whole showed a significant increase in neonatal mortality. However, when we disaggregated the main anomalies, although there was an increase in the NMR of each of the main chromosomal syndromes (Down syndrome, Edwards syndrome, and Patau syndrome), none of them was significant. If we take into account the prevalence at birth with data from the Centro de Registro de Enfermedades Congenitas at the national level, we find that there has been an increase in recent years for Edwards syndrome and Down syndrome[20], which directly affects the increase in infant deaths from these causes.

IMR and NMR due to gastroschisis presented a significant increase in the last decade. This is probably due to the increase in their prevalence, which has been described both in Costa Rica and worldwide.[21] Similarly, the group called Other specified syndromes (Q870-878), such as Siamese twins (Q894), presented a significant increase in rates. This could be due to an improvement in clinical diagnosis and therefore an increase in the number of cases, but it is a hypothesis that should be explored to determine whether the increase is due to an increase in registration as a cause of death, an increase in prevalence or mortality.

It is important to clarify that like all analyses of vital statistics, the findings are limited by the accuracy of the demographic and cause-of-death data included on child death certificates. However, vital statistics derived from national vital registration systems is an optimal source of mortality, fertility, and cause-of-death data because they are intended to cover the entire population, are available for subnational populations, and, in principle, result from a medically certified cause of each death.[22] However, in the cause-specific analysis, we see limitations arising from a lack of diagnostic specificity, for example, the group of nonspecific cardiac anomalies, which ranks second in the IMRBD.

Finally, from the findings of this analysis, it can be concluded that the downward trend in the IMRBD in Costa Rica is similar to that found in developed countries, as well as the difficulty in significantly reducing the NMRBD; and that the significant decrease in the IMRBD is due to a significant decrease in IMR and NMR due to congenital heart disease, which is the most prevalent CD in the country. Prevention measures and improvements in timely prenatal medical care and care of newborns with CD should be strengthened to contribute to a further decrease in IMR and NMR due to this cause.

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