

Prevalence of congenital malformations and deformities of the osteomuscular system in live newborns in Mexico, 2008-2017

Prevalencia de malformaciones y deformidades congénitas del sistema osteomuscular en recién nacidos vivos en México, 2008-2017

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Abstract

Background: From 2009 to 2010 in Mexico, CMDOMS prevalence was 27.4/10,000 births. The first places were congenital deformation of the feet with a prevalence of 8.0 and congenital deformation of the hip with 6.7/10,000 births. **Objective:** The objective of the study was to estimate for Mexico the national prevalence of CMDOMS in live births, by state and municipality, as well as to analyze spatial distribution by these same territorial delimitations. **Methods:** A database of 20,175,422 newborns (NB) alive from 2008 to 2017 was integrated. Percentages and prevalence were calculated at the national level, federal entities, and municipalities, with confidence intervals at 95%. Maps were made and prevalence was stratified. **Results:** The congenital malformation prevalence rate was 77.8/10,000 NB. CMDOMS were in first place with 40.8% and a prevalence of 31.8/10,000 NV. Prevalence by federal entity presented a range of 8.0-75.8/10,000 NB, were stratified by states and municipalities for presentation on maps. **Conclusion:** In Mexico for the years 2008-2017 an increase in CMDOMS prevalence was observed globally and in particular of some specific causes.

Keywords: Congenital malformations in newborns. Osteomuscular malformations. Prevalence of congenital anomalies.

Resumen

Antecedentes: En México, de 2009 a 2010, la prevalencia de las malformaciones y deformidades congénitas del sistema osteomuscular (MDCSOM) fue de 27.4 por 10,000 nacimientos. Los primeros lugares los ocuparon la deformación congénita de los pies, con una prevalencia de 8.0, y la deformación congénita de la cadera, con 6.7 por 10,000 nacimientos. **Objetivo:** Estimar para México la prevalencia nacional de MDCSOM en nacidos vivos (NV), por entidad federativa y municipio, y analizar su distribución espacial por esas mismas delimitaciones territoriales. **Método:** Se integró una base de datos de 20,175,422 NV en 2008-2017. Se calcularon porcentajes y prevalencias por ámbito nacional, entidades federativas y municipios, con intervalos de confianza al 95%. Se elaboraron mapas y se estratificaron las prevalencias. **Resultados:** La tasa de prevalencia de malformaciones congénitas fue de 77.8 por 10,000 NV. Se ubicaron en el primer lugar las MDCSOM, con un 40.8% y una prevalencia de 31.8 por 10,000 NV. Las prevalencias por entidad federativa presentaron un rango de 8.0 a 75.8 por 10,000 NV;

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se estratificaron por estados y municipios para su presentación en mapas. **Conclusión:** En México, para los años 2008-2017, se observa un incremento en las prevalencias de las MDCSOM en forma global y en particular por algunas causas específicas.

Palabras clave: Malformaciones en recién nacidos vivos. Malformaciones osteomusculares. Prevalencia de anomalías congénitas.

Introduction

Congenital abnormalities, also known as birth defects or congenital malformations (CMs), are defined as structural alterations present at birth. Their etiology can be monogenic, chromosomal, multifactorial, by potentially teratogenic environmental agents, or by malnutrition¹.

CMs are classified according to their characteristics; when there is severe biological, psychological or social involvement they are called major CMs and, otherwise, they are considered minor. The frequency of the former is 2-3% and, in stillbirths, it is 15-20%. Depending on their location, they are classified according to the affected organs or systems. Dysmorphological classification depends on the stage of prenatal life development the alteration occurs at, and on its mechanism. Malformations that originate during organogenesis are classified as malformations, deformations, or disruptions. Deformations that occur when the organogenesis period has concluded are characterized by alterations in the shape or position of affected body segments, which are secondary to mechanical forces that limit fetal movement for a prolonged period, and occur in approximately 2% of newborns. Disruptions are the result of a destructive process that alters a structure that has developed normally; they are usually sporadic².

In 2010, the World Health Organization estimated 270,000 deaths within the first 28 days of life attributed to CMs. At the 63rd World Health Assembly, regarding birth defects, countries were urged to develop a population surveillance program to accurately record congenital anomalies to have a better understanding of the impact of the morbidity of this type of pathology¹.

Efforts have been coordinated in various countries of Europe and America to obtain information on the prevalence of this type of conditions in order to generate epidemiological surveillance systems and carry out preventive actions³⁻⁵.

The methodology used to estimate the prevalence of CMs at birth is variable: surveys, hospital records

or population databases³, for a coverage of births as extensive as possible and thus obtain representative figures at both national and international level.

Congenital malformations and deformities of the musculoskeletal system (CMDMSS), grouped in the 10th edition of the International Classification of Diseases (ICD-10) within the Q65-Q79⁶ codes group, cause disability of varying magnitude, given that they compromise various functions, the degree of involvement can be severe or moderate, and have repercussions on the gross and fine motor system, as well as on sensitivity⁷.

These alterations can occur as isolated cases in families or as inherited cases and other individuals in the family may be affected, and thus familial, social, and medical care repercussions can have a bigger impact. In some cases, alterations occur in other systems, such as heart and kidney malformations, among others, which exacerbate the primary pathology, or are part of the spectrum of a specific syndrome⁷.

In Mexico, the External Malformation Registration and Surveillance Multicenter Program reported a prevalence of musculoskeletal malformations in the 1978-1985 periods of 4.69 per 1000 live births, out of a total of 248,934 live births examined⁸.

Costa Rica has a population-based CM registration system that has a coverage of more than 95% of births. During the 1995-2005 period, it reported that the group of most common malformations were those of the musculoskeletal system, which corresponded to ICD-10 Q65-Q79 codes group, with a prevalence of 69.8 per 10,000 newborns⁹.

In Hungary, skeletal alterations in 1980 had a prevalence of 2.1 per 1000 live births, ranking fourth in CMs and with 7.2% of total malformations¹⁰.

In Mexico, using ICD-10, CM global prevalence in live births and stillbirths for the 2009-2010 period was 73.9 per 10,000 births. By groups of causes, CMDMSS were ranked first, with a prevalence of 27.4 per 10,000 births; within this group, by categories, the first places were recorded by congenital foot deformation, with a prevalence of 8.0, and congenital hip deformation, with 6.7 per 10,000 births¹¹.

Table 1. Percentage and prevalence rates of total congenital malformations and group of congenital malformations and deformities of the musculoskeletal system in live births. Mexico 2008-2017

Year	Total live births	Total congenital malformations			CMDMSS group ¹			
		Cases	% in relation to total LB ²	Prevalence/10000	Cases	% in relation to		Prevalence/10000
				LB ² (95% CI ³)		total LB ²	totalCM ⁴	LB ² (95% CI ³)
2008	1,951,921	12,248	0.63	62.7 (61.6-63.9)	5,017	0.3	41.0	25.7 (25.0-26.4)
2009	2,036,946	12,990	0.64	63.8 (62.7-64.9)	5,179	0.3	39.9	25.4 (24.7-26.1)
2010	2,056,619	14,978	0.73	72.8 (71.7-74.0)	5,973	0.3	39.9	29.0 (28.3-29.8)
2011	2,026,372	15,560	0.77	76.8 (75.6-78.0)	6,467	0.3	41.6	31.9 (31.1-32.7)
2012	2,069,187	15,542	0.75	75.1 (73.9-76.3)	6,387	0.3	41.1	30.9 (30.1-31.6)
2013	2,057,594	16,209	0.79	78.8 (77.6-80.0)	6,670	0.3	41.1	32.4 (31.6-32.2)
2014	2,044,629	17,427	0.85	85.2 (84.0-86.5)	7,203	0.4	41.3	35.2 (34.4-36.0)
2015	2,020,440	17,607	0.87	87.1 (85.9-88.4)	7,164	0.4	40.7	35.5 (34.6-36.3)
2016	1,963,074	17,837	0.91	90.9 (89.5-92.2)	7,234	0.4	40.6	36.9 (36.0-37.7)
2017	1,948,640	16,489	0.85	84.6 (83.3-85.9)	6,774	0.3	41.1	34.8 (33.9-35.6)
Total	20,175,422	156,887	0.78	77.8 (77.4-78.1)	64,068	0.3	40.8	31.8 (31.5-32.0)

CI: confidence interval; CM: congenital malformations; CMDMSS: congenital malformations and deformities of the musculoskeletal system; LB: live births.

ICD-10 is a widely used instrument, since it contains classified CMs information in Chapter 17, *Congenital malformations, deformities and chromosomal abnormalities* (Q00-Q99). Live birth certificate in Mexico contains an title called CM, which is an important source for obtaining national information, by states and by municipalities, and uses ICD-10 for its coding of causes.

A literature review comprising the past 10 years about CMDMSS at birth in Mexico showed that there are no publications on this subject that break down prevalence rates by state or municipality, or their spatial distribution.

The purpose of this work was to estimate, for Mexico, the prevalence of CMDMSS in live births, nationally, by state and by municipality, as well as to analyze their spatial distribution for the same territorial delimitations.

Methods

The databases of live newborns for the 2008-2017 period available on the website of the Directorate-General of Health Information of the Ministry of Health were brought together. The working universe was made up of live births of 22-45 weeks of gestation, weighing more than or equal to 500 g and with maternal usual residence in Mexico.

Groupings of causes were made according to ICD-10, with Chapter 17, *Congenital malformations, deformities and chromosomal abnormalities* (Q00-Q99) being selected, and from it, the *Congenital malformations and deformities of the musculoskeletal system* (Q65-Q79) group of causes.

Percentages and rates of prevalence were calculated nationally, by states and by municipalities, as well as their 95% confidence intervals (CI). Maps were developed to provide a better geographical view of the indicators. Rates of prevalence were stratified using the quartile technique, and for visualization on maps, the geographic information system called Digital Map of Mexico was used, on the 6.3.0 desktop version of the National Institute of Statistics and Geography.

Results

A database of 20,175,422 live births was formed. Out of these, 156,887 had at least one CM, resulting in 0.78% for the 2008-2017 study period, with annual variations ranging from 0.63 to 0.91% for the 10-year period of analysis. Overall CM prevalence rate for the period was 77.8 (95% CI: 77.4-78.1) per 10,000 live births, with an annual range of 62.7 (95% CI: 61.6-63.9) to 90.9 (95% CI: 89.5-92.2) per 10,000 live births in the studied period (Table 1).

Table 2. Percentages by categories of the group of congenital malformations and deformities of the musculoskeletal system relative to each year's total. Mexico 2008-2017

ICD-10 Q65-Q79 group categories	2008	2017	Total 2008-2017	Percentage increase 2008 to 2017
(Q66) Congenital feet deformities	30.3	33.2	30.9	9.6
(Q65) Congenital hip deformities	24.5	22.8	24.5	-6.9
(Q69) Polydactyly	14.4	13.5	13.8	-6.3
(Q79) Congenital malformations of the musculoskeletal system, not elsewhere classified	10.0	9.8	9.9	-2.0
(Q75) Other congenital malformations of skull and face bones	3.7	4.4	4.1	18.9
(Q70) Syndactyly	3.6	3.7	3.4	2.8
(Q74) Other congenital malformations of limb (s)	3.3	2.1	2.8	-36.4
(Q67) Congenital musculoskeletal deformities of head, face, spine and chest	2.5	2.8	2.7	12.0
(Q68) Other congenital musculoskeletal deformities	1.7	2.2	1.8	29.4
(Q71) Reduction defects of upper limb	1.7	1.4	1.7	-17.6
(Q77) Osteochondrodysplasia with defects of growth of tubular bones and spine	1.5	1.3	1.5	-13.3
(Q78) Other osteochondrodysplasias	0.9	0.7	1.0	-22.2
(Q72) Reduction defects of lower limb	0.7	1.0	0.8	42.9
(Q76) Congenital malformations of spine and bony thorax	0.7	0.7	0.7	0
(Q73) Reduction defects of unspecified limb	0.5	0.4	0.4	-20.0
Total	100.0 n = 5017	100.0 n = 6774	100.0 n = 64068	--

ICD-10: International Classification of Diseases, 10th edition.

The proportion of CMDMSS relative to total live births was 0.3% in the analyzed decade, in comparison with 40.8% for total CM during the entire study period; a similar percentage was recorded in annual performance, with values ranging from 39.9 to 41.6%. The prevalence of CMDMSS for the study period was 31.8 (95% CI: 31.5-32.0) per 10,000 live births. Significant growth is observed in this indicator, with values of 25.7 (95% CI: 25.0-26.4) in the baseline year and 34.8 (95% CI: 33.9-35.6) for the past year, which represents an increase of 35.4% (Table 1).

Among the main types of CM causes, in the 10 years of analysis, CMDMSS ranked first, with 40.8%; second, congenital malformations of the eye, ear, face, and neck (Q10-Q18), with 12.6%; third, congenital malformations of genital organs (Q50-Q56), with 12.4%; fourth, cleft lip and cleft palate (Q35-Q37), with 8.1%; and fifth, congenital nervous system malformations (Q00-Q09), with 6.0%.

The main causes within the CMDMSS group (Table 2), as percentages, were congenital deformities

of feet (Q66), followed by congenital deformities of hip (Q65) and polydactyly (Q69). Together, they add up to 69.2%. With regard to the location and percentage of the other causes, no major changes were observed for each year in the analyzed decade.

By specific causes (Table 3), calculated prevalence rates of 2008 and 2017 for the three main causes with the highest absolute frequency show significant changes: congenital deformities of the feet increased their rate by 47.4%, congenital deformities of hip by 25.4% and polydactyly by 27.0%. The *Other osteochondrodysplasias* (Q78), *Congenital malformations of spine and bony thorax* (Q76), and *Reduction defects of unspecified limb* (Q73) categories maintained their prevalences unchanged. The rest of the causes, although with the lower prevalence rates than the three above-mentioned main ones, also increased their prevalence rates, with the exception of *Other congenital abnormalities of limb(s)* (Q74), which was the only one that decreased its prevalence by 12.5% (Table 3).

Table 3. Rates of the prevalence by ICD-10 Q65-Q79, Congenital malformations and deformities of the musculoskeletal system, group of categories in live newborns. Mexico 2008-2017

ICD-10 Q65-Q79 categories group	Prevalence/1000 LB ²			Percentage increase 2008 to 2017
	2008	2017	Total 2008-2017 (95% CI ¹)	
(Q66) Congenital deformities of feet	7.8	11.5	9.8 (9.7-10.0)	47.4
(Q65) Congenital deformities of hip	6.3	7.9	7.8 (7.7-7.9)	25.4
(Q69) Polydactyly	3.7	4.7	4.4 (4.3-4.5)	27.0
(Q79) Congenital malformations of musculoskeletal system, not elsewhere classified	2.6	3.4	3.1 (3.1-3.2)	30.8
(Q75) Other congenital malformations of skull and face bones	1.0	1.5	1.3 (1.3-1.4)	50.0
(Q70) Syndactyly	0.9	1.3	1.1 (1.0-1.3)	44.4
(Q74) Other congenital malformations of limb (s)	0.8	0.7	0.9 (0.8-0.9)	-12.5
(Q67) Congenital musculoskeletal deformities of head, face, spine and chest	0.6	1.0	0.9 (0.8-0.9)	66.7
(Q68) Other congenital musculoskeletal deformities	0.4	0.8	0.6 (0.5-0.6)	100.0
(Q71) Reduction defects of upper limb	0.4	0.5	0.5 (0.5-0.6)	25.0
(Q77) Osteochondrodysplasia with defects of growth of tubular bones and spine	0.4	0.5	0.5 (0.4-0.5)	25.0
(Q78) Other osteochondrodysplasias	0.2	0.2	0.3 (0.3-0.3)	0.0
(Q72) Reduction defects of lower limb	0.2	0.4	0.3 (0.2-0.3)	100.0
(Q76) Congenital malformations of spine and bony thorax	0.2	0.2	0.2 (0.2-0.2)	0.0
(Q73) Reduction defects of unspecified limb	0.1	0.1	0.1 (0.1-0.2)	0.0
Total	25.7	34.8	31.8 (31.5-32.0)	35.4

ICD-10: International Classification of Diseases, 10th edition; CI: confidence interval.

The percentage of CMDMSS by state (Table 4) varies in a range of 30.5 to 48.2%. Eleven states are above the national percentage; out of these, two are located at the north and nine in the center and west of the country. Prevalence rates by state had a wide range in the period, from 8.0 (95% CI: 7.4-8.6) to 75.8 (95% CI: 72.5-79.2) per 10,000 live births. Thirteen states had values above national prevalence: three in the north, one in the south, and nine in the center and west of the country. It is important mentioning that eight of these states also had a higher percentage of CMDMSS.

The behavior of prevalence rates by state is shown more clearly in figure 1, where the prevalence of CMDMSS by states and municipalities is stratified for presentation. Figure 1A shows that the very high and high strata form a central concentration as a corridor of the highest prevalence rates and three peripheral polarizations, with nine states (Jalisco, Colima, Aguascalientes, Guanajuato, Querétaro, Mexico City, Tlaxcala

and Puebla) being located at the central area. Of the three polarizations, one is located in the south of the country (Yucatán), another in the north (Chihuahua-Coahuila) and another in the west (Baja California).

Figure 1B shows that the spatial distribution of municipalities with higher prevalence rates that make up the very high and high strata maintain the same central concentration and polarity mentioned in the preceding paragraph, and are located within each similar stratum by state, which allows to more clearly observe the geospatial behavior of the indicator and identify those municipalities that contribute to maintaining these states with high rates of prevalence.

Discussion

The estimated overall prevalence rate of 77.8 per 10,000 live births for the 2008-2017 period could be underestimated, since internal CMs are probably not comprehensively diagnosed in the immediate neonatal

Table 4. Percentages and prevalence rates of congenital malformations and deformities of the musculoskeletal system in live newborns according to the state. Mexico, 2008-2017

Code	State	Live births	Total CM ²	CMDMSS ¹		CMDMSS prevalence per 1000 LB ³ (95% CI ⁴)
				Total	CM %	
01	Aguascalientes	256,911	4,900	1,948	39.8	75.8 (72.5-79.2)
22	Querétaro	376,728	5,550	2,492	44.9	66.1 (63.6-68.7)
29	Tlaxcala	240,299	2,743	1,314	47.9	54.7 (51.7-57.6)
09	Distrito Federal	1,218,776	14,532	6,072	41.8	49.8 (48.6-51.1)
31	Yucatán	332,431	3,959	1,468	37.1	44.2 (41.9-46.4)
13	Hidalgo	472,452	4,625	2,044	44.2	43.3 (41.4-45.1)
11	Guanajuato	1,130,671	10,979	4,742	43.2	41.9 (40.7-43.1)
06	Colima	115,324	1,414	476	33.7	41.3 (37.6-45.0)
14	Jalisco	1,394,350	13,030	5,571	42.8	40.0 (38.9-41.0)
03	Baja California Sur	117,921	1,098	468	42.6	39.7 (36.1-43.3)
05	Coahuila	550,997	4,967	1,887	38.0	34.2 (32.7-35.8)
21	Puebla	1,155,839	9,495	3,847	40.5	33.3 (32.2-34.3)
08	Chihuahua	586,266	4,866	1,898	39.0	32.4 (30.9-33.8)
	National	20,175,422	156,887	64,068	40.8	31.8 (31.5-32.0)
15	Mexico, State of	2,755,195	19,329	8,638	44.7	31.4 (30.7-32.0)
16	Michoacán	856,065	6,438	2,679	41.6	31.3 (30.1-32.5)
20	Oaxaca	633,894	5,070	1,929	38.0	30.4 (29.1-31.8)
02	Baja California	526,635	3,019	1,456	48.2	27.6 (26.2-29.1)
17	Morelos	307,364	2,008	848	42.2	27.6 (25.7-29.4)
30	Veracruz	1,190,380	8,281	3,181	38.4	26.7 (25.8-27.6)
04	Campeche	151,436	1,241	394	31.7	26.0 (23.5-28.6)
10	Durango	332,506	2,182	865	39.6	26.0 (24.3-27.7)
23	Quintana Roo	259,948	1,826	650	35.6	25.0 (23.1-26.9)
27	Tabasco	470,643	3,817	1,165	30.5	24.8 (23.3-26.2)
24	San Luis Potosí	465,680	2,979	1,140	38.3	24.5 (23.1-25.9)
28	Tamaulipas	587,079	3,697	1,375	37.2	23.4 (22.2-24.7)
18	Nayarit	200,338	1,199	466	38.9	23.3 (21.2-25.4)
12	Guerrero	561,650	3,299	1,219	37.0	21.7 (20.5-22.9)
32	Zacatecas	291,227	1,412	604	42.8	20.7 (19.1-22.4)
25	Sinaloa	492,571	2,184	764	35.0	15.5 (14.4-16.6)
26	Sonora	446,591	1,675	667	39.8	14.9 (13.8-16.1)
07	Chiapas	795,937	2,749	971	35.3	12.2 (11.4-13.0)
19	Nuevo León	829,611	1,911	667	34.9	8.0 (7.4-8.6)

CI: confidence interval; CM: congenital malformations; CMDMSS: congenital malformations and deformities of the musculoskeletal system; LB: live births.

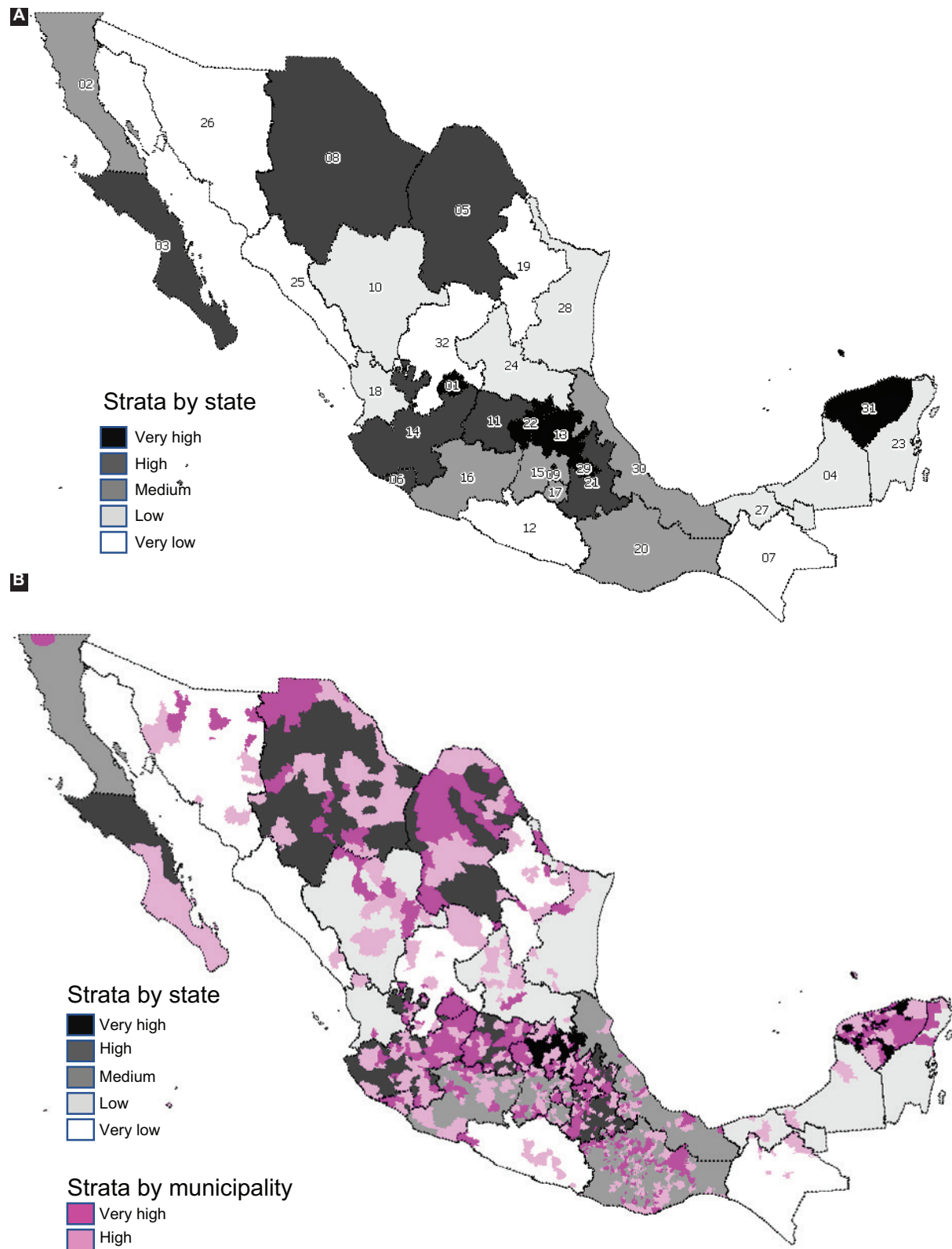


Figure 1. Geographical distribution of musculoskeletal malformations prevalence rates in live newborns, Mexico 2008-2017. **A:** stratification of states according to the rate of musculoskeletal malformations in newborns. **B:** stratification of states and municipalities very high and high strata according to the rate of musculoskeletal malformations in newborns.

period, such as malformations of the heart, lung, digestive system, kidney, uterus and appendages, and intersex states.

This article included only major or minor external musculoskeletal CMs, which are likely to have diagnostic certainty, and it can be, therefore, inferred that the prevalence rates calculated for this group of causes are highly reliable.

A previous study reported a prevalence of CMDMSS of 27.4 per 10,000 births, live and stillbirths, ranking first by groups of causes. In the 2008-2017 analysis period, CMDMSS remain at first place as CM groups for all years, with a prevalence for all 10 years of 31.8 (95% CI: 31.5-32.0) per 10,000 live births.

Costa Rica, with a population-based CM registration system similar to that of this study, reported that CMDMSS were the most common, with a prevalence of 69.8 (95% CI: 67.9-71.6) per 10,000 newborns, live, and stillbirths.

The importance of obtaining the prevalence of CMDMSS according to the ICD-10 classification recorded in birth certificates is that each code groups various pathologies with diagnoses that involve physical and functional alterations of soft tissues and bone, which will require treatments that range from conservative interventions to surgery or rehabilitation of different complexity and duration, which can prolong up to adult life and generally do not lead to a comprehensive recovery.

In the 2008-2017 analysis periods, there is a trend towards an increase when absolute and prevalence frequencies are considered, globally and in particular for some specific causes. Among the latter, deformities of hip and feet, of multifactorial etiology, which affect ambulation and body position, and which make up a total of 55.4%, stand out for their high prevalence, as well as polydactyly and syndactyly with autosomal dominant etiology, of variable expression in most cases, with a total of 17.2%, which can be resolved with minimal intervention or require a highly specialized management of hand or foot surgery, with esthetic or functional repercussions.

Both these groups, which have a clear genetic influence of multifactorial and autosomal dominant etiology, add up to 72.6%, and could be considered with familiar genetic risk and would require genetic counseling in order to inform on risks of recurrence and offer prevention. This coupled with the fact that in other groups there are alterations that have a genetic etiology and that would increase the specified percentage.

From the medical care point of view, head, and face malformations, when occurring with functional and

esthetic compromise, require highly specialized, and interdisciplinary surgical treatments; as for spinal and bony thorax malformations, they can compromise growth, body stability and respiratory function and require permanent medical surveillance.

Reduction defects of limbs are extremely serious malformations that significantly alter motor skills, as well as body integrity. They account for 2.9% and have a prevalence of 0.5 (95% CI: 0.5-0.6) in upper limbs, and in lower limbs, 0.3 (95% CI: 0.2-0.3) per 10,000 live births. Regarding osteochondrodysplasias, they will cause skeletal, soft tissue, and height alterations, with an impact on affected sites function. They can be part of specific syndromes with different genetic etiology, such as achondroplasia, which is autosomal dominant and can involve familiar presentation.

The significant percentage increase of 42.9 in reduction defects of lower limbs (Q72) in the 2008-2017 period draws the attention, since such an increase was not observed in reduction defects of upper limbs or unspecified limb.

The states with the highest prevalence rates are practically concentrated in the center of the country. When prevalence rates by municipality are overlapped, spatial distribution changes, as the areas with the highest risk are identified at the center, north and south of the Republic.

The spatial pattern of CMDMSS prevalence rates, where strata with high and very high prevalence rates, in the analysis carried out both by states and municipalities, are concentrated in the center of the country, with some polarizations located in the south, north and northwest of the country, should be highlighted. Although this geographical distribution allows to identify the priority states and municipalities for carrying out medical care actions for these health problems, it is advisable to investigate the reasons why this conglomeration occurs and find to the extent possible the fundamental causes, to allow additional preventive actions to be carried out.

Conflict of interests

The authors declare that there are no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this investigation.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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