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Congenital Malformations of the Central Nervous System in Rural Western Honduras: A 6-Year Report on Trends

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Abstract

Background—Central nervous system (CNS) malformations including neural tube defects (NTDs) are the second most common type of birth defects world-wide, and are major causes of childhood disability and mortality. We report the first analysis of prevalence in Western Honduras of CNS malformations including NTDs over six consecutive years.

Methods—Data from all patients with congenital CNS malformations and total live births between 2010 and 2015 were obtained through institution and regional registries from all three public referral hospitals in Western Honduras, representing 67 municipalities. Cases were identified using the ICD-10 CNS malformation codes. Birth prevalence was calculated as cases per 10,000 live births.

Results—Overall, 275 cases of CNS malformations were identified from 123,903 live births (54% Females, 58% NTDs). Overall 6- year birth prevalence of CNS malformations ranged from 13.9 and 31.1. Spina bifida variants and anencephaly represented 80% and 19% of reported NTDs, respectively. Total 6-year prevalence of NTDs in Western Honduras ranged from 7.0 to 17.4 over years studied. Six municipalities demonstrated average prevalence over 30 (maximum 49.0).

Conclusion—This is the first study reporting disease-burden of CNS malformations in Western Honduras. The nationwide birth-prevalence of NTDs in rural Honduras may have decreased since the implementation of prenatal health policies started in 2005. However, we identified regions with unexpectedly elevated prevalence, indicating high regional prevalence that could be targeted for improved preventative efforts, ultimately decreasing the burden of these conditions.

Keywords

Congenital Malformations of the CNS; Folic Acid; Honduras; Neural Tube Defects; International Neurosurgery

Introduction

Birth defects are one of the significant causes of infant mortality globally and estimated to cause 376,000 deaths in children younger than 5 years and 24 million disability-adjusted life years (DALYs) worldwide.^{1–3} Among birth defects, neural tube defects (NTDs), a spectrum of central nervous system (CNS) malformations, are considered important contributors of childhood disability and death particularly among low- and middle income countries (LMICs).⁴ In LMICs, studies show that 17% to 70% of neonatal deaths from birth defects are attributed to NTDs, and the malformations are also associated life-long burden of disease.^{4–6}

Among NTDs, spina bifida (myelomeningocele) and anencephaly are the most common presentations affecting humans, although less common variants (lipomyelomeningocele, diastematomyelia, occult spinal dysraphism, and craniorachischisis) may also be present at birth.^{7–8} The birth prevalence of NTDs is about 10 in 10,000 live births but is also reported to have global variation with limited studies in LMICs.^{9–12} The birth prevalence of NTDs in African nations as reported in the literature ranges from 5.2 to 75.4 per 10,000 live births and prevalence in Latin American countries ranges from 2.1 to 96.3 per 10,000 live births.^{9, 12} However, many of these studies in LMICs settings suffer from limitations including lack of continued active surveillance or representing single institution reports. Most of this variation, particularly in LMICs, is largely attributed to differences in primary prevention with folic acid through food fortification or supplementation, however genetic predisposition may play a significant role.⁴ Birth prevalence of NTDs also has observed variation across time, country, region, race, and ethnicity.^{7, 11–12}

In Honduras, a 1-year retrospective review in six urban hospitals showed that 49% of deaths associated with birth defects were due to NTDs.¹³ Population-based surveillance for NTDs is not only essential in determining disease burden, but is invaluable in identifying potential significant regional variations and guiding national and regional control strategies. However, there are no population-based surveillance systems for NTDs in Honduras and data on the NTD birth prevalence data have been only obtained from two limited studies.^{9, 12–14} It is also unclear what the impact of recent attempts to create folic acid fortification policies in Honduras, and whether these are widely adopted. We report birth-prevalence estimates for CNS malformations, including NTDs, over six consecutive years in rural Western Honduras

Materials and Methods

This study is a descriptive analysis of the birth prevalence estimation for CNS malformations, including NTDs, in Western Honduras. Institutional review board approval for this descriptive analysis was obtained from both Hospital de Occidente de Honduras and Vanderbilt University Medical Center.

We define Western Honduras as the region formed by three departments (Copan, Lempira, and Ocotepeque). The region's healthcare infrastructure is composed by a total of three public hospitals and two large private clinics that serve as secondary and tertiary care centers with each municipality having a primary care community clinic. Hospital de Occidente, located in Santa Rosa de Copan, serves as the major tertiary care referral center for the region. Specialty care for the entire region is available at Hospital de Occidente with some services available within the private sector. This hospital also has the main neurological surgery services available to the region with the only available neurosurgeon who operates both in this hospital and also one of the private facilities since 2009. Cases requiring higher level of care, such as birth defects, are mostly all referred to Hospital de Occidente with only a few cases presenting to one of the two private clinics with higher level care capabilities. Data from the total number of live births within the region, including in and out of hospital births, between 2010 and 2015 were obtained through regional birth registries established through the Ministry of Health and used for all national statistics in all three departments within Western Honduras. Data included stratification by department and by each of the 67 municipalities within the region used for mapping prevalence. Data on all cases of CNS malformations and NTDs were obtained through chart review on all newborn admissions with CNS malformations or NTDs from each of the three public Hospitals within the region, including both those born within the hospital or those admitted after birth at home or in a community center. Data included baseline demographics as well as disease specific information and outcomes. Inclusion criteria was all in-hospital births, newborns, or children admitted after out-of-hospital-birth since 2010 with a birthdate between 2010 and 2015 with CNS malformations. Cases were identified using the International Classification of Diseases, 10th Revision (ICD-10). Codes used for inclusion criteria were as follows: Q00 (Anencephaly and similar malformations), Q01 (Encephalocele), Q02 (Microcephaly), Q03 (Congenital Hydrocephalus), Q04 (Other congenital malformations of the brain), Q05 (Spina bifida including hydromeningocele, meningocele, meningomyelocele, myelocele, myelomeningocele, rachischisis, spina bifida, syringomyelocele), Q06 (Other congenital malformations of the spinal cord), Q07 (Other congenital malformations of nervous system). Codes Q00-Q07 were used for the identification of all CNS malformations while Q00, Q01 and Q05 were used to identify NTDs.

Of a total of 435 cases with reported admission since 2010 identified using ICD codes Q00-Q07, 362 were born between 2010 and 2015 and met inclusion criteria. A query for duplicate records using medical record numbers identified 61 duplicate records which were excluded from birth prevalence calculations. Of the remaining 301 cases, 26 of them belonged to departments outside the three departments within our defined region and were thus excluded. No cases belonged to patients from neighboring countries.

A population-based estimate of birth-prevalence was calculated as cases per 10,000 live births. Some municipalities with just a few cases during the six-year period had years with no cases. For this reason, at the municipality level, we report six-year prevalence only. Birth-prevalence for each year is reported for departments and for the region. Data cleaning, analysis, and time-series graphs were conducted using STATA 14. A geographic information system (GIS) (ArcGIS 10.3.1; Esri; Redlands, CA, USA; <http://www.esri.com/software/arcgis>) was used to create a map based on estimates of birth-prevalence by municipality.

Administrative boundaries were obtained from DIVA-GIS Free Spatial Data (<http://www.diva-gis.org/gdata>) and the Honduras Instituto Nacional de Estadística (INE).

Results

In total, 275 cases of CNS malformations were identified out of 123,903 live births within the region between 2010 and 2015. Most patients identified were affected with NTDs (57%) (Table 1). Of the patients with NTDs, spina bifida variants and anencephaly represented 80% and 19% respectively. According to the vital status on the records from their last admission, 25% of patients were reported dead while 6% had missing information on vital status. Out of the 56,608 total births reported for Copan alone between 2010 and 2015, 53% were in-hospital births and 32% were births within municipal primary care centers, while 14% were home births. Hospital de Occidente reported 224 and 122 cases of CNS malformations and NTDs respectively.

The 6-year birth prevalence estimates for the region were 22 and 13 for CNS malformation and NTDs respectively (Table 2). Copan had the highest 6-year prevalence estimate (24) for CNS malformations while Lempira had the highest 6-year prevalence estimate (16) for NTDs. A time-series graph by year for birth prevalence of CNS malformations and NTDs in Western Honduras demonstrates the annual variation (Figure 1 and Table 3). The prevalence of CNS malformations ranged between 14 and 31 while that of NTDs ranged from 7 to 17 between 2010 and 2015. While initially showing a downward trend, 2015 had the second highest reported prevalence. A similar graph by year for each of the three department within the region shows an increase in birth prevalence of NTDs in 2015 which primarily attributed to increases in Lempira and Ocotepeque (Figure 2 and Table 3).

Mapping of the 6-year prevalence by municipality for both CNS malformations and NTDs for each of the 67 municipalities within the region corrected for live-births within each municipality show six that demonstrated average birth prevalence of NTDs greater than 30 with a maximum of 49 (Figure 3). Three of these high-prevalence municipalities are from Copan (San Jose, San Pedro, and Trinidad) and three in Lempira (Cololaca, Talgua, and Valladolid). There were no cases recorded for 23 municipalities during the 6-year period of this study: 8 out 16 municipalities in Ocotepeque, 9 out of 28 municipalities in Lempira, and 6 out of 23 municipalities in Copan.

Discussion

We describe the 6-year birth prevalence as well as regional patterns in of CNS malformations including NTDs in Western Honduras and uncovered regional patterns of higher than expected prevalence. Six municipalities of potential concern were identified that could be targeted with public health interventions to reduce the higher birth prevalence of NTDs. The regional variations observed may be explained by access to health care, particularly prenatal care, and health literacy. Areas of lower prevalence, particularly from municipalities near Guatemala and El Salvador may represent an artifact and our study most likely underestimates true birth prevalence in those municipalities. We were conservative in our estimation of birth-prevalence and included in our calculations total births that occurred

within municipalities with no cases reported during the 6-year period. It is expected that with this approach estimated birth-prevalence will be lower than true birth-prevalence in the region because of health seeking behaviors along the borders. Patients from areas with no cases reported or those with low prevalence are likely to seek healthcare from out of the country or other cities in Honduras. Population-based studies are absent in Honduras and there has been no description of birth defects in this region. The only two studies describing birth prevalence of NTDs in Honduras relied on data from major city and peripheral hospitals. The first one reported a birth prevalence 22.3 per 10,000 live births between 1998–2000 in a single-center retrospective study.¹³ The second study reported a birth prevalence of 24.3 per 10,000 live births and was a stronger study that included several national public hospital, including rural regions, between 2000–2001.¹⁴ However, it wasn't until 2003 that mandatory fortification of wheat flour with folic acid was legislated in all Central America.¹⁵ This same year, the Ministry of Health of Honduras approved the use of folic acid for all women of childbearing age for the prevention of birth defects, however, the norm did not start implementation until 2005.^{16–17} Since these regulation changes occurred, there have been no follow up studies assessing the impact of recently adopted health policies and regulations targeting reduction of NTDs in Honduras. It is also unclear how widely adopted these policies and regulations have been. We report here findings from the first study following implementation of national regulations of folic acid fortification and supplementation. Estimates on birth-prevalence from this study are lower than those reported in the two prior studies. While this could represent that supplementation efforts have had an impact, it is also possible that this represents an underestimation of a higher prevalence than reported in this study. Even if it did represent a reduction, true comparison is not possible because the only two prior studies are hospital-based and may not be representative of this region. Nicaragua, El Salvador, and Guatemala are three neighboring countries with similar socio-political status, however, data is only available for Guatemala. National birth-prevalence in Guatemala according to these reports ranges between 22.8 and 31.6 with single hospital registries reporting birth-prevalence as high as 88.6.^{9, 12} These are similar to the birth-prevalence in municipalities with higher prevalence from our study and may be more representative of true prevalence within Western Honduras.

It is well established that folic acid supplementation during the preconception period reduces the reduce risk of NTDs.¹⁸ National folic acid fortifications strategies have been proven as effective methods to reduce prevalence of NTDs.¹⁹ In Latin America, comparison of pre- and post-fortification prevalence is only available for six countries, all with higher socio economic status, and show 33–59% reduction in prevalence. Prior studies on blood folate levels in Honduran women of child bearing age showed that while there are regional variations, blood folate levels in all locations were in the low normal range when compared to the pre-supplementation/pre-fortification US population.²⁰ One study assessing folic acid knowledge, attitudes, and practices in Honduras through surveys reported that only approximately half of the respondents (46.4%) had heard of folic acid and just over one-third (37.6%) knew that it was a vitamin related to preventing birth defects.¹⁷ This supports the implementation of policies geared towards improved prenatal care and supplementation in Honduras. While it is possible that genetic predisposition may play a role on the variation we observed, these most likely represent variations in folic acid fortification and

supplementation and access to adequate prenatal care. Therefore, policies and interventions should first focus on primary prevention for this region.

Our study has several limitations. Ascertainment of cases is difficult in LMICs, data repositories are non-existent or less than perfect and we were forced to rely on a retrospective design which likely caused us to miss cases and underestimate birth prevalence. Medical records are paper-based in Honduras and prone to coding and documentation errors which may also have caused patients to be excluded. A few cases may have presented to one of the two existing private clinics in the region, however, Hospital de Occidente functions as the major referral center for the region, especially for patients with requiring specialty care, this explains why most of the cases reported (77%) in this study were from this hospital. Western Honduras borders two other countries, Guatemala and El Salvador, and patients are likely to seek healthcare outside the country. For example, prior to 2009, there were no local neurological surgeons serving the region and patients with neurosurgical conditions would have to travel to one of the two major cities in Honduras, outside of the country, or forgo treatment. Today, the only Neurosurgeon in the region works mostly in the public sector. Some of these health-seeking patterns still persist and may explain why some areas show lower than expected prevalence, particularly in municipalities that are near international borders. It is also possible that a significant number of cases may not even seek healthcare which is not uncommon in LMICs, especially for those who die shortly after birth. However, at least in Copan, 85% of total births within the region occurred within the healthcare infrastructure and unlikely to significantly impact prevalence estimations. Our prevalence calculations for the region were done with a conservative approach which included live births from all municipalities and, therefore, is most likely represents an underestimation of true disease burden in the region.

Conclusions

The prevalence of NTDs and CNS malformations in rural Honduras may have decreased slightly since the implementation of fortification and supplementation policies in 2005. However, we identified municipalities with higher than expected birth prevalence suggesting that these policies may not be widely adopted or may even suggest a genetic predisposition. These areas could be targeted for improved health education, promotion, and prevention to significantly decrease the burden of disease. Further studies are needed to evaluate why some areas were found to have higher than expected birth-prevalence and to assess the impact of prevention strategies in Honduras.

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Abbreviations list

CNS	Central Nervous System
DALYs	Disability-adjusted life years

GIS	Geographic Information System
ICD-10	International Classification of Diseases, 10th Revision
INE	Instituto Nacional de Estadística
LMICs	Low and Middle Income Countries
NTDs	Neural Tube Defects

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Highlights

- Birth-prevalence estimates from 2010 through 2016 for congenital malformations of the central nervous system including neural tube defects for three departments in Honduras (Western Honduras) are reported.
- The estimated birth-prevalence of congenital malformations of the central nervous system ranged between 14 and 31 per 10,000 live births while that of neural tube defects ranged from 7 to 17 per 10,000 live births between 2010 and 2015 for the region.
- Six municipalities are identified that show estimated birth-prevalence higher than 30 per 10,000 live births for neural tube defects.

Figure 1. Birth prevalence of CNS malformations and NTDs in Western Honduras
Prevalence patterns of CNS malformations and NTDs in Western Honduras from 2010 through 2015. Prevalence is reported as cases per 10,000 live births.

Figure 2. Birth prevalence of NTDs in Western Honduras by Department

Prevalence patterns of neural tube defects (NTDs) by each of the three departments comprising Western Honduras from 2010 through 2015. Prevalence is reported as cases per 10,000 live births.

Figure 3. Mapping of 6-year birth prevalence of CNS malformations and NTDs in Western Honduras by Municipality

Map shows of the 6-year prevalence ranges of CNS malformations (A) and NTDs (B) in all municipalities in Western Honduras. Areas of higher prevalence (>30) are shown in black in black. Also shown are the main hospital serving the region (Hospital del Occidente) and two peripheral hospitals serving the region (Hospital de Gracias and Hospital de San Marcos). Prevalence is reported as cases per 10,000 live births.

Table 1

Demographics

	NTD (N=158)	CNS Malformations (N=275)
Gender		
Males, n (%)	60 (37.97)	126 (45.82)
Females, n (%)	98 (62.03)	149 (54.18)
Reporting Institution		
Western Hospital, n (%)	122 (77.22)	224 (81.45)
Regional Hospital in Lempira, n (%)	19 (12.03)	29 (10.55)
Regional Hospital in Ocotepeque, n (%)	17 (10.76)	22 (8)
Cases by Department (State)		
Copan, n (%)	67 (42.41)	138 (50.18)
Lempira, n (%)	72 (45.57)	107 (38.91)
Ocotepeque, n (%)	19 (12.03)	30 (10.91)
ICD 10 Codes		
Q00 Anencephaly, n (%)	30 (18.99)	30 (10.91)
Q01 Encephalocele, n (%)	2 (1.27)	2 (0.73)
Q02 Microcephaly, n (%)		35 (12.73)
Q03 Congenital Hydrocephalus, n (%)		72 (26.18)
Q04 Other Cong. Mal. Of Brain, n (%)		10 (3.64)
Q05 Spina Bifida, n (%)	126 (79.75)	126 (45.82)
Q06 Other Cong. Mal. Of Spinal Cord, n (%)		0 (0)
Q06 Other congenital malformations of nervous system, n (%)		0 (0)
Cases by Year		
2010, n (%)	33 (20.89)	59 (21.45)
2011, n (%)	26 (16.46)	40 (14.55)
2012, n (%)	24 (15.19)	43 (15.64)
2013, n (%)	16 (10.13)	32 (11.64)
2014, n (%)	28 (17.72)	47 (17.09)
2015, n (%)	31 (19.62)	54 (19.64)
Outcomes		
Dead, n (%)	40 (25.32)	63 (22.91)
Alive, n (%)	109 (68.98)	199 (72.36)
Unkown, n (%)	9 (5.70)	13 (4.73)

6-year prevalence in Western Honduras of NTDs and congenital malformations of the CNS

Table 2

Department (State)	Live Births	Neural Tube Defects		CNS Malformations	
		Cases	Prevalence per 10,000 live births (95% CI)	Cases	Prevalence per 10,000 live births (95% CI)
Copan	56,926	67	11.77 (9.2–14.84)	138	24.24 (20.45–28.54)
Lempira	48,481	72	14.85 (11.71–18.58)	107	22.07 (18.18–26.55)
Ocotepeque	18,496	19	10.27 (6.40–15.70)	30	16.22 (11.17–22.83)
Western Honduras	123,903	158	12.75 (10.88–14.86)	275	22.19 (19.69–24.93)

Birth prevalence of NTDs in Western Honduras per year (per 10,000 live births)

	Copan	Lempira	Ocoateque	Western Honduras			
	Prevalence per 10,000 live births						
Year	NTDs			Spina Bifida	Anencephaly	Encephalocoele	NTDs
2010	15.17	24	9.84	15.83	1.58	0	17.42
2011	10.56	15.37	9.95	11.46	0.96	0	12.42
2012	10.07	14.31	3.23	9.5	1.36	0	10.86
2013	6.05	6.15	12.33	5.24	1.75	0	6.99
2014	22.12	9.12	6.68	10.74	3.76	0.54	15.04
2015	7.48	22.68	19.31	9.32	5.39	0.49	15.91