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ORIGINAL ARTICLE

Incidence of congenital malformations of the central nervous system in newborns in Chiapas, Mexico, and associated factors

*Norberto Enríquez-Vera[1], Fernando Ruiz-Balbuena[1,2], Mauricio Megchún-Hernández[3], and Alfredo Briones-Aranda[4]**

[1]Departamento de Enseñanza e Investigación, Hospital "Dr. Jesús Gilberto Gómez Maza" SSA, Tutxtla Gutiérrez; [2]Facultad de Ciencias Odontológicas y Salud Pública, Universidad de Ciencias y Artes de Chiapasp, Tutxtla Gutiérrez; [3]Departamento de Pediatría, Hospital de Especialidades Pediátricas, Tutxtla Gutiérrez; [4]Facultad de Medicina Humana, Universidad Autónoma de Chiapas, Tuxtla Gutiérrez. Mexico

Abstract

Introduction: *Malformations of the central nervous system (CNS), the type of congenital defect second only to cardiac malformations, cause infant disability and mortality.* **Objective:** *The aim of the study was to evaluate the incidence of congenital malformations of the CNS in newborns treated at a regional public hospital in Southern Mexico and explore the associated factors.* **Methods:** *This descriptive study included 113 newborns with CNS malformations. A specific diagnosis was provided and information was obtained from the parents in relation to age, schooling, occupation, prenatal control, intake of folic acid, and exposure to pesticides. A database was created in the statistical program Epi Info version 3.4.3 to carry out univariate and bivariate analyses using the Chi-square test, with significance considered at $p < 0.05$.* **Results:** *The most frequent malformations were hydrocephalus (45.1%), Arnold-Chiari (32.7%), and encephalocele (8.0%). Of the 113 newborns herein examined, a greater percentage of congenital malformations was found when the first pregnancy took place in mothers 12-19 versus over 19 years of age (78.8% vs. 21.2%, respectively; $p < 0.05$). Furthermore, 40.2% of mothers were exposed to insecticides and 39.8% to herbicides and/or fungicides before or during pregnancy. Only 15.4% of the mothers consumed folic acid during the first trimester of pregnancy.* **Conclusion:** *The incidence of congenital abnormalities of the CNS in newborns is a serious problem, perhaps associated with exposure of the mother to pesticides and a deficient intake of folic acid. Therefore, it is necessary to strengthen prenatal care and health literacy to help reduce the occurrence of these disorders.*

Keywords: *Congenital malformations. Risk factors. Central nervous system. Folic acid. Pesticides.*

Incidencia de malformaciones congénitas del sistema nervioso central y factores asociados en recién nacidos de Chiapas, México

Resumen

Introducción: *Las malformaciones congénitas del sistema nervioso central (SNC) son el segundo defecto congénito más común después de las malformaciones cardiacas y pueden asociarse a mortalidad y discapacidad infantil.* **Objetivo:** *estudiar la incidencia de las principales malformaciones congénitas del SNC y factores asociados en recién nacidos atendidos en un hospital público de segundo nivel en Tuxtla Gutiérrez, Chiapas.* **Métodos:** *estudio descriptivo, que incluyó a 113 recién nacidos con malformaciones del SNC. Se precisó el diagnóstico, se obtuvo información de los padres: edad, escolaridad, ocupación, control prenatal, ingesta de ácido fólico, exposición a plaguicidas. Se integró una base de datos en el programa*

***Correspondence:**
Alfredo Briones-Aranda
E-mail: alfredo.briones@unach.mx

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estadístico Epi Info versión 3.4.3, se realizó un análisis univariado y bivariado mediante la prueba chi cuadrada y un valor $p < 0.05$ se consideró un resultado significativo. **Resultados:** *las malformaciones más frecuentes fueron: hidrocefalia (45.1%), Arnold-Chiari (32.7%) y encefalocele (8.0%). El porcentaje de casos fue más elevado (78.8%) en madres cuyo primer embarazo fue entre los 13 y 20 años ($p < 0.05$). El 40.2% de las madres durante el embarazo estuvieron expuestas a insecticidas y 39.8% a herbicidas y fungicidas. Únicamente el 15.4% de las madres consumieron ácido fólico durante el primer trimestre del embarazo.* **Conclusión:** *es grave y preocupante la alta incidencia de anormalidades congénitas del SNC, lo cual podrían estar asociado con la exposición de plaguicidas y deficiencias en la ingesta de ácido fólico. Consecuentemente se necesita fortalecer la atención prenatal y la alfabetización en salud para coadyuvar en la disminución de estos padecimientos.*

Palabras clave: *Malformaciones congénitas. Sistema nervioso central. Ácido fólico. Plaguicidas.*

Introduction

Central nervous system (CNS) anomalies appear to be the most common systemic congenital anomalies, with an incidence of about 1%[1-3]. In low-income countries, 17-70% of neonatal deaths resulting from birth defects are attributed to neural tube defects (NTDs)[4]. Unfortunately, the information available on birth defects in Latin America is scarce and fragmented, indicating inadequate epidemiological surveillance. This information is a vital element for the proper monitoring and evaluation of the impact of prevention and intervention programs. Hence, the ability to adequately assess efforts aimed at reducing the incidence of NTDs in the total births per year (~11 million) is hindered[5].

Moreover, the etiology and mechanisms of fetal CNS abnormalities are still poorly understood. One report has estimated that ~40% of pathogenic factors may be genetic and environmental[6]. As an example of the environmental factor, human exposure to pesticides takes place by direct contact with sprayed crops, through consumption of residues in food and water, and during or after indoor/outdoor application[7]. Various studies have found an association between exposure to organophosphates during fetal development and early childhood and adverse neurodevelopmental effects[8-10].

Regarding the preventative strategies to diminish CNS anomalies, various clinical trials have evidenced the importance of periconceptional folic acid intake to reduce the occurrence of NTDs in newborns[11]. According to long-term surveillance of NTDs in countries that have successfully implemented fortification (e.g., the United States, Canada, Costa Rica, South Africa, and Chile) and data from a supplementation program in China, folic acid intervention strategies can apparently decrease the incidence rate of NTDs to as low as 5-6 cases per 10,000 pregnancies[12-14]. However, epidemiological surveillance of NTDs and other birth defects is still limited worldwide[15]. The objective of the current contribution was to evaluate the annual incidence (2014) of congenital abnormalities of the CNS in newborns treated at a regional second-level public hospital in Tuxtla Gutiérrez, Chiapas, Mexico, and explore some factors that may be associated with this serious problem.

Materials and methods

During 2014, a descriptive study of a population of 113 newborns was carried out in a second-level hospital, the Regional Public Hospital "Dr. Rafael Pascacio Gamboa", in the City of Tuxtla Gutiérrez, the State of Chiapas, Mexico. The diagnosis of each case with a congenital abnormality of the CNS was made by a certified neurosurgeon (the main author of the current report). A questionnaire was developed to explore diverse factors possibly associated with the incidence of NTDs. The sociodemographic factors included the age and education of the parents as well as the type of maternal prenatal control. An evaluation was also made of the maternal intake of folic acid (the dose and whether it began in the periconceptional stage or the first or second trimester of pregnancy) and maternal exposure to distinct types of pesticides (insecticides, herbicides, and fungicides). The questionnaire, expressly elaborated for this investigation, consisted of concrete, closed-ended, and categorical questions accompanied by mutually exclusive response options. Before its application to study participants, a pilot study was conducted with a sample of 25 mothers to test the validity and reliability of the different sections of questions (data not shown). Hence, the final version of the instrument was understandable and coherent.

This research was authorized by the Institutional Research Committee and also by its Bioethics Committee. Care was taken to maintain the anonymity of the participants.

Once the information was collected, a database was created in the statistical program Epi Info version 3.4.3. For each type of variable, a univariate descriptive analysis was carried out to calculate the average and the corresponding percentage. With such information, the general characteristics of the sample could be identified relative to each variable. Subsequently, a bivariate analysis was conducted to reveal the extent of the correlation between the sociodemographic and independent variables, using Pearson's Chi-square statistic and considering significance at $p < 0.05$.

Results

The results included in the present study were 113 newborns with a diagnosis of congenital malformations of the CNS, of which 55 were boys (48.6%) and 58 girls (51.4%). The diagnosis with the greatest incidence was hydrocephalus, with 51 cases (45.1%), followed by Arnold-Chiari malformation and encephalocele with 37 and 9 patients (32.7% and 8.0%), respectively (Table 1).

The number and percentage of congenital malformations of the CNS in the newborns under study were analyzed in relation to each of the sociodemographic variables of the fathers and mothers (Table 2). A significant association was found between most of the sociodemographic variables of the parents of the newborns (age of each parent during the pregnancy, educational level of the father, and the type of prenatal care) and the existence of a congenital malformation of the CNS. The exception was the lack of relation with the educational level of the mother.

Although the majority of both parents was over 19 years old, the mothers 12-19 years of age during the first trimester of pregnancy corresponded to 78.8% of the newborns with congenital malformations of the CNS. Likewise, the majority of parents had over 6 years of schooling and prenatal control attended by a doctor, but the ones without these characteristics presented the highest percentage (71.7%) of newborns with congenital malformations of the CNS (Table 2).

The number and percentage of mothers of newborns with a congenital abnormality of the CNS were classified with respect to the time at which folic acid intake began (Table 3). Folic acid supplements were consumed by 77 of the 113 mothers interviewed (68.1%). However, 41 of these mothers (36.2%) started taking this treatment during the second trimester of pregnancy, while 17 (15.4%) did so during the first trimester. Only six of the mothers (5%) took folic acid supplements during the 3 months before pregnancy (Table 3).

Positive substance dependence (alcoholism and/or smoking) was manifested in 99 fathers (87.6%) and 21 mothers (18.6%). On the other hand, 34 mothers (30.4%) were exposed to insecticides before pregnancy and 46 (40.2%) during pregnancy. Likewise, 45 mothers had contact with herbicides and one with fungicides (a total of 39.8%) (data not shown).

Table 1. Distribution of the type of congenital defect of the CNS in the newborns under study

Diagnosis	n (%)
Hydrocephalus	51 (45.1)
Arnold Chiari malformation	37 (32.7)
Encephalocele	9 (8.0)
Anencephaly	4 (3.5)
Lipomeningocele	4 (3.5)
Hydroanencephaly	2 (1.8)
Meningocele	2 (1.8)
Total	113 (100.0)

n: the number of each malformation found.

Table 2. Analysis of the sociodemographic variables of the fathers and mothers of newborns with congenital abnormalities of the central nervous system

Variable	Number (%)	χ^2; p
Age of the mother (years)		
12-19	32 (28.3)	20.2; 0.0003
≥ 20	81 (71.7)	
Age of the father (years)		
12-19	9 (8.0)	35.2; 0.0001
≥ 20	104 (92.0)	
Age of the mother (years) during her first pregnancy		
12-19	89 (78.8)	21.2; 0.0001
≥ 20	24 (21.2)	
Years of schooling: Father		
≤ 5 years	49 (43.4)	3.98; 0.04598
≥ 6 years	64 (56.6)	
Years of schooling: Mother		
≤ 5 years	62 (54.9)	2.14; 0.14335
≥ 6 years	51 (45.1)	
Type of prenatal control		
Doctor	48 (71.7)	55.84; 0.0000
Mixed	12 (17.9)	
Midwife	7 (10.4)	

A significant association (Chi-squared test (χ^2); $p < 0.05$) between congenital defects and the sociodemographic variables is indicated in bold type.

Discussion

The high number (113 cases) of congenital malformations of the CNS detected in the present study is

Table 3. Distribution of mothers according to intake of folic acid supplements

Time at which folic acid intake began	n (%)
Over 3 months before pregnancy	6 (5.0)
0-3 months before pregnancy	8 (7.0)
During the 3rd trimester	17 (15.4)
During the 1st trimester	41 (36.2)
During the 2nd trimester	5 (4.4)
Total	77 (68%)

n: the number of cases.

alarming. The current data contrast sharply with that found in the report of the epidemiological surveillance system of neural tube and craniofacial defects (SVEDTN/DCF) for 2020 in relation to the State of Chiapas, which identified only 45 cases, corresponding to an incidence of 33.3 cases per 100,000 newborns[16]. This could be due to certain failures in the compilation of information by the national health system.

One of the strengths of the present study was the timely diagnosis of the 113 newborns encountered in daily medical practice in a second-level hospital, which demonstrates the feasibility of planning and executing observational research in similar clinical scenarios to provide key insights that can improve healthcare.

The most frequent diagnoses, in descending order, were hydrocephalus, Arnold-Chiari malformation, and encephalocele. According to the SVEDTN/DCF, hydrocephalus was one of the most frequent malformations in 2020 at the national level as well, followed by microcephaly and ODD[17]. Similar findings have been described in other Latin American countries, especially in Colombia, where hydrocephalus was one of the most frequent congenital anomalies[18-21].

Another similarity with national reports became apparent when analyzing the proportion of congenital abnormalities in regard to the gender of the children. In the present study, congenital malformations of the CNS were disproportionately concentrated among female versus male newborns (58% vs. 42%, respectively)[22]. Likewise, the SVEDTN/DCF figures indicate that abnormalities at the national level were greater in female than male newborns in 2012 (51% vs. 46%, respectively)[22], a trend also observed in 2020[16].

On the other hand, the proportion of cases was higher in children when the first pregnancy of their mother had taken place from 12 to 19 versus over 19 years of age (78.8% vs. 21.2%, respectively). In contrast, the greatest percentage of congenital abnormalities at the national level was in newborns from mothers from 20 to 24 year old, followed by those between 15 and 19 years of age[16]. This difference is probably associated with the high incidence of teenage pregnancies registered in the State of Chiapas[23].

Concerning the capacity of folic acid intake to reduce NTDs, the timing of folic acid consumption is critical, being most effective when it begins during the periconceptional period (as of at least 1 month before pregnancy) and continuing to the end of the first trimester[24-26]. Unfortunately, the practice of most mothers in the current sample was not consistent with the aforementioned indications. Only 7.8% of the mothers started taking folic acid supplements 3 months before pregnancy, while 15.4% and 36.2% did so during the first and second trimester of pregnancy, respectively. Hence, the majority of mothers who gave birth to a child with a CNS abnormality had an inadequate consumption of this food supplement, which is probably related, at least in part, to deficiencies in the application of existing prenatal care programs of the Secretary of Health in Mexico. Consequently, it is essential to strengthen the application of these programs and at the same time promote health literacy.

Moreover, the considerable percentage of mothers presently evaluated who were exposed to pesticides (40.2%), herbicides, and fungicides (39.8%) during pregnancy points to toxicity as a possible cause of congenital malformations of the CNS. A study carried out in Paraguay found the following factors to be associated with this type of malformation: Living next to fumigated fields (OR = 2.5; p = 0.02) or < 1 km away from these (OR = 2.7; p = 0.008), the storage of pesticides at home (OR = 15.4; p = 0.003), and direct or accidental contact with pesticides (OR = 3.2, CI = 95%; p = 0.04)[27].

The main weakness of the current contribution is the lack of information about the specific pesticide to which the mothers were exposed and the degree of exposure or the quantity of the toxic substance in the blood of the mother or the newborn. However, this weakness creates an opportunity for the future research in rural and urban areas, with the aim of gaining further insights into the hypotheses herein posed.

CNS malformations are a complex group of disorders that are being increasingly studied and diagnosed. Unfortunately, developing countries like Mexico face a complex reality for early diagnosis and follow-up of such malformations. The limited implementation of health programs due to the lack of government funding likely constitutes a key element involved in the slow progress of prevention[28], early diagnosis, and health education. Several articles have emphasized the importance of prenatal care for the application of new strategies (e.g., fetal ultrasonography, fetal magnetic resonance imaging, and amniocentesis with advanced genetic techniques) to achieve an early diagnosis of these abnormalities[29].

In conclusion, the alarmingly high number of congenital malformations of the CNS presently found in newborns in Chiapas could be associated with exposure to pesticides and/or a deficient folic acid intake. It is necessary to strengthen prenatal care and health literacy programs to contribute to the reduction of such disorders.

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None.

Conflict of interests

None.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

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. Right to privacy and informed consent. The authors have obtained approval from the Ethics Committee for analysis and publication of routinely acquired clinical data and informed consent was not required for this retrospective observational study.

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