Original Article

Prevalence and factors associated with congenital malformations in live births

Prevalência e fatores associados às malformações congênitas em nascidos vivos

Prevalencia y factores asociados a las malformaciones congénitas en nacidos vivos

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Abstract

Objective: To estimate the prevalence of congenital malformations and to identify associated factors in live births.

Methods: Cross-sectional study, population-based, with data from the Live Births Information System. A bivariate statistical analysis (Chi-square test) and a multivariate statistical analysis (multiple logistic regression) were performed to evaluate the association between the variables and the outcome (live-births with or without congenital malformations).

Results: A total of 346,874 live births were registered, of which 3,473 presented some type of congenital malformation, with an average prevalence of 1.0%. In the multiple analysis, the factors positively associated with prevalence were: duration of pregnancy less than 37 weeks (OR = 1.17), maternal age between 20 and 29 years (OR = 0.893), singleton pregnancy (OR = 1.775), type of delivery (OR – 0.827), and number of prenatal consultations inferior to six (OR = 1.214).

Conclusion: The variables pointed out in the study integrated a predictive model that can help in the planning of health services, suggest hypotheses regarding etiological factors, and finance prenatal care actions with attention to the identified factors.

Resumo

Objetivo: Estimar a prevalência de malformações congênitas e identificar os fatores associados em nascidos vivos.

Métodos: Estudo transversal, de base populacional, com dados do Sistema de Informações sobre nascidos vivos. Procedeu-se a uma análise estatística bivariada (teste Qui-quadrado) e multivariada (regressão logística múltipla) para avaliar a associação entre as variáveis e o desfecho (nascidos vivos que possuem ou não malformações congênitas).

Resultados: Registraram-se 346.874 nascidos vivos, desses 3.473 apresentaram algum tipo de malformação congênita, com prevalência média de 1,0%. Na análise múltipla os fatores, positivamente associados à prevalência foram: duração da gestação menor que 37 semanas (OR= 1,17), idade materna entre 20 e 29 anos (OR= 0,893), tipo de gravidez única (OR= 1,775), tipo de parto (OR= 0,827) e consultas de pré-natal inferior a seis (OR= 1,214).

Conclusão: As variáveis apontadas no estudo integraram um modelo preditivo que pode auxiliar no planejamento dos serviços de saúde, sugerir hipóteses sobre os fatores etiológicos, e subsidiar as ações do pré-natal com atenção para os fatores identificados.

Keywords
Congenital abnormalities; Vital statistics; Health information systems; Live birth; Prevalence

Descritores
Anormalidades congênitas; Estatísticas vitais; Sistemas de Informação em Saúde; Nascido vivo; Prevalência

Descriptores
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Resumen

Objetivo: Estimar la prevalencia de malformaciones congénitas e identificar los factores asociados en nacidos vivos.

Métodos: Estudio transversal, de base poblacional, con datos del Sistema de Información sobre nacidos vivos. Se procedió a un análisis estadístico bivariado (prueba χ^2 de Pearson) y multivariado (regresión logística múltiple) para evaluar la relación entre las variables y el resultado (nacidos vivos que tienen o no tienen malformaciones congénitas).

Resultados: Se registraron 346.874 nacidos vivos, de los cuales 3.473 presentaron algún tipo de malformación congénita, con prevalencia promedio de 1,0 %. En el análisis múltiple, los factores asociados de forma positiva a la prevalencia fueron: duración de la gestación menor a 37 semanas (OR= 1,17), edad materna entre 20 y 29 años (OR= 0,893), tipo de gestación única (OR= 1,775), tipo de parto (OR= 0,827) y consultas de atención prenatal inferiores a seis (OR= 1,214).

Conclusión: Las variables observadas en el estudio integran un modelo predictivo que puede ayudar a la planificación de los servicios de salud, sugerir hipótesis sobre los factores etiológicos y respaldar las acciones de la atención prenatal con énfasis en los factores identificados.

Introduction

Congenital malformations are a major cause of infant impairment and mortality, especially during the neonatal period, and constitute a significant and growing clinical and public-health challenge, due to the impact on the health of the population.[1,2] In the world, it is estimated that 2 to 5% of newborns have some type of malformation and about 303,000 die during the neonatal period.[1,3] In many low- and medium-income countries, congenital malformations are not considered a public health priority and are perceived by the medical community as rare and unavoidable events.[4]

Congenital malformations are defined as functional and structural changes in embryonic or fetal development, resulting from genetic, environmental, or unknown causes, which may be identified during the prenatal period, at birth, or, occasionally, later during childhood.[1,5,6] In their etiology, are found infections (*Cytomegalovirus* infection, rubella, and toxoplasmosis), genetic factors (hereditary), environmental factors (maternal medical conditions, substance abuse, infection, medications, radiation, hyperthermia, exposure to chemical products, air pollution, solvents, pesticides, heavy metals, and uterine abnormalities).[3,7] In addition to these, there are other known risk factors, such as maternal age, smoking, chronic diseases, gestational diabetes, obesity, and new threats, as the *Zika virus* epidemic, which offers a favorable setting for increasing congenital malformations.

Another indirect determinant of congenital malformations is low income, around 94% of severe malformations occur in low- and medium-income countries. As an indirect determinant, this greater risk is related to the possible lack of access to nutritious and sufficient food by pregnant women, to greater exposure to agents or factors such as infection and alcohol, or less access to health care.[1]

In Brazil, the general prevalence does not differ from the one found in other regions of the world, which reaches approximately 2 to 5% of all live births.[5,8-11] A recent case-control study conducted in the country identified an incidence of 3.2% and pointed out as the main risk factors the occurrence of relatives with the same congenital malformation, maternal alcohol consumption, gestational diabetes, and previous miscarriages.[4] Similar to what was observed in other countries, the research conducted locally has shown the association between malformations and the use of agrochemicals.[12] In addition to the aforementioned factors, the national emergency caused by the *Zika virus* associated with microcephaly increased the occurrence of malformations in Brazil,[13] Pernambuco being considered as the epicenter state of the epidemic, due to the elevated number of cases.[13]

In the state of Pernambuco, a research on the epidemiological profile of newborns with congenital malformation identified a proportion of 0.8%.[14-17] In the city of Recife (PE), malformations constitute one of the main causes of infant mortality, especially during the neonatal period. To know its prevalence, the nature of the occurrence, as well as the associated factors is important for the early diagnosis, planning, and resource allocation for specialized health services, contributing to the improvement of quality of life and reduction of infant mortality. From this perspective, the objective of this study was to estimate the prevalence of congenital malformations and identify the associated factors in live births in Recife, Pernambuco, from 2001 to 2015.

Methods

This was a cross-sectional epidemiological observational study conducted from the data of live births with congenital malformations, of mothers residing in Recife (PE), from 2001 to 2015. The city had a population of 1,617,183 in 2015,[18] covering a territorial extent of 218,435 km^2, and a population density of 7,039.64 people/km^2.

The data source was the Information System on Live Births – Sinasc.[5] This system was deployed in 1990 and aims to gather information on births in the national territory.[16] Data on live births are collected through the Live Birth Certificate (LBC). The presence of a congenital malformation at birth came to be registered in the LBC in 1999, being described and coded according to the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10). In 2011, a new version of the LBC was distributed throughout the country, with changes in the fields related to the collection of information on congenital malformations.[17]

The variables were selected, dichotomized (except maternal age), and grouped according to the newborn characteristics: sex ("female" or "male"), birth weight ("<2,500 grams" or "≥2,500 grams"), and Apgar score at one minute ("<7" or "≥7") and at 5 minutes ("<7" or "≥7"); maternal characteristics: age ("<20 years" or "20-29 years", or "≥30 years"), educational level ("<8 years" or "≥8 years"); pregnancy characteristics: type of pregnancy ("singleton" or "multiple"), number of prenatal consultations ("<6" or "≥6"), and duration of pregnancy ("<37 weeks" or ≥37 weeks); and delivery: type of delivery ("vaginal" or "cesarean").

The prevalence of congenital malformations per year (number of live births with malformation/total number of live births in the same period x 100) and the average prevalence rate for the analyzed period were calculated. The variation rate for the initial value was calculated for the variables number of live births, number of live births with congenital malformations and malformation prevalence, according to the following formula: Δ% [(Final year-Initial year)/Initial year]×100, in which, if the value is greater than 1, there was an increase in the indicator for the final year in relation to the initial, and in case it is inferior to 1, a decrease occurred. The average prevalence rate was estimated from the sample mean. The growth rate was calculated using the values in the lowest possible level of approximation to obtain more reliable results.

An analysis of the completion of the variable "congenital anomaly detection" and the other variables of the study was performed before the statistical analysis. Then, a bivariate statistical analysis was performed, using the Chi-square test to identify associations between the study variables and the target event that, in this case, is the presence or absence of congenital malformations in live births. Subsequently, a multiple logistic regression model was adjusted, calculating the odds ratio (OR) for each studied factor, allowing the understanding of which can be considered of risk or protection.

The investigated factors (independent variables) were: sex, birth weight, Apgar score in the 1st minute and the 5th minute of life, age, maternal educational level, type of pregnancy, number of prenatal consultations, duration of pregnancy, and type of delivery. All calculations and analyses were performed using the R language version 3.2.2 for Windows and the stipulated level of significance was of 5%.

The study project was approved by the Research Ethics Committee of the Fundação Joaquim Nabuco (CAAE: 67399617.6.0000.5619).

Results

346,874 live births were notified in Recife from 2001 to 2015, 3,473 of which presented some type of congenital malformation and 329 (0.1%) did not present this information. The annual average prevalence was 1.0%, with a maximum of 1.4% in 2015 and a minimum of 0.7% in 2012. The variation rate for the initial value of live birth with congenital malformations prevalence was 21% in the considered period, and there was an increase of 13.2% in the number of congenital malformation cases during the period (Table 1).

Table 1. Distribution of live births and prevalence of congenital malformations

Year	Number of live births	Number of live births with CMF	Prevalence of live births with CMF (%)
2001	25,294[a]	296	1.2
2002	24,307[b]	207	0.9
2003	24,676[c]	275	1.1
2004	22,898[d]	250	1.1
2005	23,207[e]	227	1.0
2006	22,646[f]	240	1.1
2007	22,046[g]	204	0.9
2008	22,261[h]	184	0.8
2009	22,546[i]	215	1.0
2010	21,796[j]	225	1.0
2011	22,218[k]	178	0.8
2012	22,633[l]	151	0.7
2013	23,176[m]	224	1.0
2014	23,506[n]	262	1.1
2015	23,664[o]	335	1.4
Total	346,874	3,473	1.0
Δ%	-6.4	13.2	21

CMF - congenital malformation; LB - live births. Proportion of live births with the information regarding congenital malformation ignored: a) 0.18%; b) 0.10%; c) 0.09%; d) 0.21%; e) 0.05%; f) 0.07%; g) 0.03%; h) 0.01%; i) 0.08%; j) 0.03%; k) 0.14%; l) 0.15%; m) 0.03%; n) 0.05%; o) 0.08%

On live births with congenital malformations, there was a predominance of males (60.1%), with birth weight ≥2.500g (77.3%), satisfactory Apgar scores in the first and fifth minutes (68.4% and 86.6%). The mothers were between 20 and 29 years old (49.1%), with eight or more years of education (65.3%), with a singleton pregnancy (97.5%), had less than six prenatal consultations (52.9%), with a duration of pregnancy of 37 or more weeks (78.9%), and gave birth to their children through a cesarean section delivery (55.5%) (Table 2).

Regarding the sex variable, there was lower prevalence of females (OR=0.70; CI 95%=0.65-0.75). It was found a higher chance of anomalies in premature infants with gestational age under 37 weeks (OR=1.17; CI 95% 1.04-1.32) and in newborns with birth weight lower than 2,500 g (OR=2.093; CI 95% 1.86-2.36), and unsatisfactory Apgar in the 1st (OR=1.825; CI 95% 1.67-2.00) and 5th minute (OR=3 CI 95% 2.64-3.41). An association between single pregnancies (OR=1.775; CI 95% 1.41-2.23) and the vaginal type of delivery (OR=0.827; CI 95% 0.77-0.89) was observed. There was an association of congenital malformation cases for those mothers who had less than six prenatal consultations (OR=1.214; CI 95% 1.13-1.31) (Table 3).

Table 2. Newborn, maternal, pregnancy, and delivery characteristics, according to the presence of congenital malformation

Characteristics	Malformation Yes No. (%)	Malformation No No. (%)	p-value
Sex[a]			< 0.001*
Female	1310(39.9)	160296(48.9)	
Male	1974(60.1)	167694(51.1)	
Birth weight (grams)[b]			< 0.001*
<2.500	745(22.7)	28204(8.6)	
≥2.500	2539(77.3)	299786(91.4)	
Apgar 1st minute[c]			<0.001*
<7	1039(31.6)	44221(13.5)	
≥7	2245(68.4)	283769(86.5)	
Apgar 5th minute[d]			<0.001*
<7	439(13.4)	7257(2.2)	
≥7	2845(86.6)	320733(97.8)	
Maternal age[e] (in complete years)			0.003*
< 20	663(20.2)	62962(19.2)	
20-29	1611(46.0)	170666(52.0)	
≥ 30	1010(30.8)	9436(28.8)	
Educational level (years)[f]			0.011*
<8 years	1140(34.7)	106991(32.6)	
≥8 years	2144(65.3)	220999(67.4)	
Type of pregnancy[g]			0.085
Singleton	3201(97.5)	321167(97.9)	
Multiple	83(2.5)	6823(2.1)	
Prenatal consultation[h]			< 0.001*
<6	1736(52.9)	146588(44.7)	
≥6	1548(47.1)	181402(55.3)	
Pregnancy duration (in weeks)[i]			< 0.001*
<37	693(21.1)	29950(9.1)	
≥37	2591(78.9)	298040(90.9)	
Type of delivery[j]			0.001*
Vaginal	1459(44.4)	155571(47.4)	
Cesarean	1825(55.5)	172419(52.6)	

*The Null Hypothesis was rejected, because the *p*-value is smaller than the significance level of 0.05 (5%). Proportion of live births with information ignored: a) 0.04%; b) 0.02%; c) 0.8%; d) 0.5%; e) 0.06%; f) 1.2%; g) 0.04%; h) 1.4%; i) 0.5%; j) 0.05%

Discussion

The results of the study showed a reduction in the number of live births. However, there was an increase in the occurrence and proportion of live births with congenital malformation. An average prevalence of malformations of 1.0 case per 100 live births was estimated. The multiple analysis had as factors positively associated with the prevalence: low birth weight, unsatisfactory Apgar score in the 1st and 5th minute of life, singleton pregnancy, number of prenatal consultations inferior to six, premature birth (<37 weeks), and type of delivery. This information is relevant for monitoring, prevention, and improvement of specialized care.

Table 3. Odds ratio, confidence interval, and significance adjusted by the multiple logistic regression, according to variables that describe the newborn, maternal, pregnancy, and delivery characteristics

Variable	Odds ratio (adjusted)	Confidence interval (95%)	p-value
Sex			-
Female	0.70	(0.65-0.75)	<0.001*
Male	1	-	-
Birth weight (grams)			
< 2,500	2.09	(1.86-2.36)	<0.001*
≥ 2,500	1	-	-
Apgar 1st minute			
<7	1.82	(1.67-2.00)	<0.001*
≥7	1	-	-
Apgar 5th minute			
<7	3	(2.64-3.41)	<0.001*
≥7	1	-	-
Maternal age (in complete years)			
< 20	0.92	(0.83-1.02)	0.115
20-29	0.89	(0.82-0.97)	0.006*
≥30	1	-	-
Educational level (years)			
<8 years	1.05	(0.98-1.14)	0.181
≥8 years	1	-	-
Type of pregnancy			
Singleton	1.77	(1.41-2.23)	<0.001*
Multiple	1	-	-
Prenatal consultation			
<6	1.21	(1.13-1.31)	<0.001*
≥6	1	-	
Pregnancy duration (in weeks)			
<37	1.17	(1.04-1.32)	0.012*
≥37	1	-	-
Type of delivery			
Vaginal	0.82	(0.77-0.89)	<0.001*
Cesarean	1	-	-

*The Null Hypothesis was rejected, because the *p*-value is smaller than the significance level of 0.05 (5%).

Initially, an analysis of the quality of the Sinasc database used in this study is needed. The quality of information on live births is indispensable for monitoring malformations. The absence of completion of the variable "detection of congenital malformation" was 0.1%. Furthermore, for the other variables, the percentage of incompleteness (ignored + blank) was considered excellent. The highest percentages were for the maternal educational level and the number of prenatal consultations variables, with a percentage below 1.5%. Sinasc is a system with coverage above 90% in most units of the federation, it is reliable[16] and has high completeness of the variables.[19] Similarly, the studies conducted in the state of Pernambuco and the city of Recife have shown improvement in the adequacy of the information of Sinasc.[5,20]

Specifically for the variable "detection of congenital anomaly", the research that evaluated the attributes and the usefulness of Sinasc in Brazil showed a percentage of information ignored of 2.5. The analysis of this same variable performed for Recife verified 99.9% of completeness[5] Cosme et al.[10] state that the correct completeness of this variable allows to examine de frequency of congenital malformations, in order to develop reliable indicators of health, applicable to the planning of child health policies. High quality data are essential to generate information for public health actions and the monitoring of congenital malformations.[21,22]

An average prevalence of 1.0 case per 100 live births (1.0%) was estimated. The prevalence identified by the study resembles those of other cities and states of the country. In the city of Salvador (BA), the prevalence was 1.0%, 1.6% in São Paulo (SP), 0.9% in the state of Rio Grande do Sul, and 0.58% in Rio Grande do Norte.[10,11,23] These variations may be due to seasonal, environmental, and regional differences, or to the lack of detection of some cases of malformations.[24] The causes of malformations are complex and include several risk factors, such as maternal age, exposure during pregnancy, geographic location, race/color, and ethnicities.[3]

In this study, the highest prevalence of live births with malformations occurred in the year 2015. Possibly, these results are related to the increase in the number of newborn infants with microcephaly in Brazil, which became an epidemic and caused the Ministry of Health to declare a national public health emergency situation.[25] In the state of Pernambuco, an increase in live births with microcephaly related to the *Zika virus* was observed and the highest concentration of cases was in the city of Recife.[26] The identification of these cases demonstrates the importance of Sinasc for monitoring of congenital malformations and the need to improve the monitoring system of congenital malformations.[27]

Regarding the multiple logistic regression model, the variables associated with the risk of developing some type of congenital malformation were: low birth weight (<2,500 g) and Apgar score in the 1st and 5th minute of life, maternal age, type of pregnancy, number of prenatal consultations, premature birth (<37 weeks), and type of delivery. Premature birth, low birth weight, and unsatisfactory Apgar score were associated in the study with congenital malformations. Manifestly, there is an association of malformations with intrauterine growth restriction and low birth weight.[28,29] The research that analyzed the birth weight per gestational age and congenital malformations identified the parity, the low birth weight, the gestational age under 35 weeks, male sex and lack of prenatal care as the most significant risk factors for congenital malformations.[30] Nhoncanse et al.[31] observe that premature birth, low weight, and low Apgar score in the 1st and 5th minutes in live births with congenital malformations contribute to infant morbidity and mortality.

In this study, maternal age between 20 and 29 years was the most frequent and shows association, however, presenting lower chances of malformations than the other age groups. There is a known association between advanced maternal age and a significantly higher risk of chromosome abnormalities and miscarriage, potentially caused by the ovarian aging process, increasing the meiotic nondisjunction rate.[29] Women with advanced maternal age present higher rates of incidence of comorbidities (gestational diabetes, pregnancy-induced hypertension, among others) and their newborn infants have higher chances of congenital malformations.[10,32] The identification of pregnant women with higher risk to have an adverse pregnancy outcome allows greater monitoring, clinical follow-up, and targeted prenatal care.

Less than six prenatal consultations attended were associated with congenital malformations in live births. Other studies also pointed out a smaller number of prenatal consultations as a factor associated with birth with congenital malformations.[30,33] The organization of good prenatal consultations, the strengthening of primary health care, and the folic acid supplementation are simple but effective prophylactic measures to prevent congenital malformations.[34] The beginning of the prenatal follow-up during the first weeks of pregnancy and the attendance at the recommended number of consultations allows the early detection of fetal alterations, as well as prevents the exposure to environmental and teratogenic factors.[35]

A statistical association with the singleton pregnancy has been demonstrated. However, it has been observed the predominance of congenital malformations in multiple pregnancies.[10] The higher number of cases of congenital abnormalities in multiple pregnancies can be explained, in part, by errors during cell division (genetic factors), chromosomal abnormalities, intrauterine environmental factors, and amniotic sac or umbilical cord constriction.[10]

Some limitations must be considered when interpreting the results of the study. The cross-sectional nature prevents the establishment of any cause-and-effect relationship between the malformations and the variables analyzed. The use of secondary data that may be underreported presents classification errors and incompleteness of information. However, the analysis of the completeness showed low incompleteness proportion. To detect congenital abnormalities, a thorough and careful systematic clinical and physical examination performed by the pediatrician at birth is necessary and must be more emphasized. The results justify the relevance of the study by providing a representative image of the congenital abnormalities load among live births. Additionally, the multiple analysis allowed an inference on the variables associated with congenital malformations.

Conclusion

The final model of explanation for congenital malformations in live births in Recife was composed of: premature birth, low birth weight, Apgar score in the 1st and 5th minute and under seven, singleton pregnancy, vaginal delivery, and less than six prenatal consultations attended. Knowledge regarding the prevalence and the factors associated with congenital malformations can contribute to the planning of maternal and child health actions, the improvement of diagnostic methods, specialized follow-up with measures that improve quality of life, increase survival time, and reduce infant mortality in Recife. The elaboration of prevention strategies, early detection, and treatment of congenital malformations is fundamental for reducing infant morbidity and mortality.

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Collaborators

Gonçalves MKS and Bonfim CV contributed with the conceptualization of the study, data analysis and interpretation, and writing of the manuscript and approve the final version to be published. Cardoso MD and Lima RAF contributed with the critical review of its intellectual content and approve the final version to be published. Oliveira CM contributed with data analysis and interpretation, writing of the manuscript, and approves the final version to be published.

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