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Factors associated with congenital differences in neonates in southern Benin: a case-control study

Abstract

Background: Congenital differences are one of the major causes of morbidity and mortality in neonates. Their etiology is multifactorial including a combination of genetic and environmental factors. This study aimed to investigate the factors associated with congenital differences in neonates in southern Benin.

Methods: We conducted a case-control study over a six-month period. Cases were neonates with congenital differences. A neonate of the same sex and gestational age, whose mother is the same age and parity as a case, who did not have any congenital difference, was considered a control. Data were extracted from registries and medical record. Analyses were performed using logistic regression models.

Results: Seventy-eight cases were recorded out of the 3,534 newborns hospitalized, giving a hospital rate of 2.2%. They were matched with 147 controls. Digestive malformations (20.5%), congenital heart disease (16.7%) and anterior abdominal wall malformations (16.7%) were the main deformities observed. Factors associated with the occurrence of congenital differences were father's age (p=0.013), mother's origin (p=0.010), parity (p=0.029) and pregnancy follow-up (p=0.010). Mortality due to congenital malformations was 35.9%.

Conclusion: Congenital differences should be assessed in all regions to determine their prevalence, nature and associated factors, so that specific preventive measures can be taken.

Keywords: congenital differences, associated factors, neonate, mortality, Benin

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Introduction

The birth of a child with a permanent disability is experienced as a real tragedy given both the mysticoreligious considerations surrounding it and the burden it places on families.[1] Congenital malformations are one of the main causes of neonatal morbidity and mortality. The World Health Organization (WHO) estimates that congenital malformations affect around 1 in 33 newborns, causing some 3.2 million disabilities every year.[2] The etiology of these malformations is multifactorial including a combination of genetic and environmental factors. Awareness of these risk factors would enable action to reduce their incidence and subsequently reduce neonatal and infant mortality rates. This study aimed to investigate the factors associated with congenital differences' occurrence in southern Benin.

Methods

This study was approved by the Research Ethics Committee of the Faculty of Health Sciences in Cotonou. A case-control study was carried out to achieve our objective. The study was conducted over a six-month-period, from January 01 to June 30, 2022. It took place in the neonatal units of the two largest referral university hospitals for the management of congenital malformations. Both hospital are located in the southern Benin. These two hospitals strive to offer cutting-edge obstetric, neonatal and pediatric surgical care in the country. One hospital also has a medical genetics department.

All neonates hospitalized in the neonatology units of the two referral university hospitals were enrolled. Cases were neonates with congenital differences or chromosomal abnormalities among live births hospitalized in neonatal care units and for whom one parent (father or mother) had given informed consent. A neonate of the same sex and gestational age, whose mother is the same age and parity as a case, and whose parent (father or mother) has given informed consent, but who did not have any congenital difference, was considered a control.

For cases, we exhaustively recruited all neonates admitted during the study period for congenital differences.[3,4] Controls were neonates born in the same month as the case, who met our matching criteria and whose parents consented to participate in the study.

The odds ratio between cases and controls was 3. The risk of the first degree was 5% and the risk of the second degree was 20%. The ratio of the case to control was 1:2. The proportion of exposed subjects among cases was 2.7%. The proportion of exposed controls was 4.5%. The proportion of exposed cases was 0.9%.[5] The final sample size was 206 neonates (69 cases for 138 controls).

The data collection techniques used were tabulation and individual interview. The interview was conducted with the parents (father or mother) to complete data extracted from registries and medical record (socio-demographic data and family history).

A questionnaire containing socio-demographic, clinical, therapeutic and outcome parameters was filled in from the files. This data collection form was pre-tested on twenty neonates at another hospital, in order to address any inconsistencies. Data were collected by the same investigator. The questionnaire was digitized for digital data collection, then administered to both groups.

At the end of data collection, the database was cleaned to check completeness and consistency. Data analysis was carried out using R 4.1.1 software. Proportions were calculated for qualitative variables. Quantitative variables were expressed as mean and standard deviation for those with a normal distribution, while the median and interquartile range (Q1; Q3) were calculated for quantitative variables with an asymmetric distribution. The normality of the distribution was verified using the Shapiro test.

For multivariate, we performed a binary logistic regression using the top-down stepwise method. The threshold for variable retention after univariate logistic regression analysis was 20%. The association between the identified factors and the variable of interest was determined by the odds ratio (OR) and its 95% confidence interval [CI95%]. Adjusted measures of association were generated using the "*Broom*" and "foresmodel" packages, and presented in a table. The selected significance level was 5% ($p<0.05$).

Results

Seventy-eight cases were identified out of 3,534 hospitalized neonates, accounting for a hospital rate of 2.2%. They were compared with 147 control neonates. Single malformations were the most frequent in 73.1% of cases. Digestive malformations (20.5%), congenital heart disease (16.7%) and abdominal wall malformations (16.7%) were the main malformations encountered (Table 1).

Table 1 Pattern of malformations encountered

Type of malformations	n= 78	
Digestive malformation	**16**	**20,5**
Neonatal obstruction	5	6,4
Hirschsprung's disease	4	5,1
Anorectal malformation	3	3,8
Esophageal atresia	2	2,6
Diaphragmatic hernia	2	2,6
Cardiac malformations	**13**	**16,7**
Cyanogenic congenital heart disease	8	10,3
Non-cyanogenic congenital heart disease	5	6,4
Abdominal wall defects	**13**	**16,7**
Omphalocele	8	10,3
Gastroschisis	3	3,8
Prune belly	1	1,3
Bladder exstrophy	1	1,3
Head and face malformation	**9**	**11,5**
Cleft lip and palate	4	5,1
Choanal atresia	2	2,5
Microcephalia	1	1,3
Anophtalmia	1	1,3
Pierre Robin's syndrome	1	1,3
Orthopedic malformations	**7**	**9,0**
Club foot	5	6,4
Polydactyly	1	1,3
Spine deformities	1	1,3
Nervous system defects	**7**	**8,9**
Spina bifida	3	3,8
Hydrocephalus	3	3,8
Encephalocele	1	1,3
Urogenital malformations	**5**	**6,4**
Disorder of sex development	3	3,8
Cryptorchidia	2	2,6
Down's syndrome	6	7,7
Amniotic band disease	2	2,6
Others	**8**	**10,3**

Mothers between 20-37 of age were predominantly represented (88.5%). Mothers were not well-educated in 28.2% of cases, and 48.7% were housewives or traders. Parents lived in the countryside in 30.8% of cases. Only one mother had a family history of congenital difference. Multiparity accounted for 24.3%, and the median parity was 2.5 deliveries, with quartiles of 1.0 and 4.5 for mothers of malformed newborns. During pregnancy follow-up, 65.4% of mothers had poor compliance with prenatal care, with fewer than 4 prenatal consultations. Only 17.9% of pregnant women had undergone a morphology ultrasound in the second trimester, and only 04 pregnant women were diagnosed with congenital differences. Good pregnancy follow-up involved at least 04 antenatal visits and a morphology ultrasound in the 2nd trimester. In our series, 17 women out of 225 (7.6%) surveyed had good pregnancy follow-up (Table 2). Two-thirds of the newborns were born at term and vaginally. They were predominantly male, with a sex ratio of 55.1%, and their median weight was 2,700 g. Mortality due to congenital malformations was 35.9% (Table 3).

Table 2 Maternal characteristics and age of fathers

	Case (n=78)	Control (n=147)
Mother's age: Avg ± SD	28,20 ± 5,81 years	27,12 ± 5,62 years
Father's age : Med + IQ	37,5 years IQ: 30 – 42,5 years	35 years IQ: 28,5 – 41 years
Multiparity	24,3%	15%
Rural residence	30,8%	16,3%
Gestational age : Med + IQ	37 WA* IQ : 36,5 – 38 WA	38 WA IQ : 35,5 – 39 WA
Prenatal consultations < 4	65,4%	70,1%
Antenatal ultrasound	17,9%	4,8%
Good pregnancy follow-up	14,1%	4,1%

*weeks of amenorrhea

Table 3 Newborns features

	Case	Control
Male gender	55,1%	57,1%
Weight: Med + IQ	2,7 Kg IQ : 2,1 – 2,9 Kg	2,8 Kg IQ : 2,2 – 3,2 Kg
Neonatal resuscitation	16,7%	19%
Mortality	35,9%	-

In the multivariate model, factors associated with congenital differences after multiple logistic regression were young paternal age, maternal residence, multiparity and poor pregnacy follow-up (Table 4).

Table 4 Factors associated with congenital malformations: multivariate analysis

	Congenital malformations (Case/ Control)		
	ORa*	CI 95%	p-value
Father's age			
<20	1		
20 – 37	0,47	[0,26-0,85]	0,013
>37	1,00	-	
Mother's residence			
Urban	1		
Rural	2,44	[1,24-4,81]	0,010
Parity			
Primiparous (1)	1		
Multiparous (4-5)	2,34	[1,09-5,05]	0,029
Good pregnancy follow-up			
Yes	1		
No	3,85	[1,36-10,87]	0,010

*Adjusted odds ratio

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Discussion

The hospital incidence of congenital malformations was 2.2%. This was higher than the 0.9% and 1.68% reported respectively by Atinnonkpon et al[5] in 2016 in six hospitals in southeastern Benin and Tchente Nguefack et al between 2008 and 2012 in Cameroon.[4] On the other hand, higher proportions have been reported in several other studies. These include De Vigan[6] in France (3.2%), Lubala[1] in Lubumbashi, Congo (6.8%) and Hama[7] in Niger (7.85%). These variable incidences could be explained by the diversity of study methods used by the authors. But it nevertheless shows that congenital malformations are not rare and remain a current concern.

In our series, single-malformations were the most common (73.1%). These results are similar to those of Youl and Mayanda, who found 80.3% and 76.9% mono-malformations respectively.[8,9] Among these single-malformations, malformations of the digestive tract predominated. Garçon et al. in Haiti reported similar findings with 37.5% of malformations of the digestive tract and 19.8% of malformations of the abdominal wall.[10] Teixeira de Aguiar in Portugal found a predominance of limb anomalies respectively.[11] This difference in distribution could be due to the fact that non-life-threatening orthopedic malformations would not systematically lead parents to seek care. In our study, the proportion of congenital malformations increased significantly with the young age of the fathers. Kazaura et al had found the same association, with fathers under 20 years of age having 1.3 times the risk of having a child with congenital malformation.[12] Zhu in the United States found that, compared with fathers aged between 20 and 29, the risk of malformations was significantly increased by 37% in the case of fathers aged over 45.[13] In our study, mothers living in rural areas were 2.44 times more likely to have a child with congenital malformation in their offspring. The use of pesticides in rural areas could explain this finding. Hama et al found a preponderance of congenital malformations in rural areas.[7] The use of pesticides and herbicides in rural agriculture could explain this finding. According to COGNEZ,[14] in an exposed unexposed cohort study, exposure to pesticides increased the risk of urological malformations such as hypospadias and cryptorchidism. On the other hand, Kaboré et al describe a high frequency of congenital anomalies in urban environments.[15] But none of these studies established a statistically significant link between place of residence and the occurrence of congenital malformations. The multiparous women in our study were more exposed to the occurrence of congenital malformations. They were 2.34 times more likely to have a child with congenital malformation than primiparous women. The effect of parity on the occurrence of congenital malformations is not clearly defined. Some studies incriminate primiparity in the emergence of congenital malformations. LASSEGUE Epogo's study in Morocco associates a high malformative risk with primiparous mothers.[16] But for Rabah et al, it is multiparity that is incriminated.[17] With regard to pregnancy monitoring, only 7.6% of mothers had good monitoring of their pregnancy. This mediocre result could be explained by parents' lack of financial resources for consultations. Downe et al[18] established the relationship between social inequalities and pregnancy monitoring. For him, the first consequence of maternal poverty is inadequate monitoring of pregnancies. According to Vrijheid et al,[19] there is a gradient between the risk of congenital anomalies, which increases as the poverty index rises. We found that poor pregnancy monitoring increased the risk of having a malformed newborn by 3.85 times. Radouani et al[20] in Morocco in 2011 demonstrated that poor pregnancy monitoring led to neural tube closure anomalies. This is thought to be due to a lack of folic acid taken periconceptionally or at the start of pregnancy, a deficiency of which would favour such congenital anomalies.

Conclusion

Congenital malformations account for a significant proportion of neonatal morbidity and mortality. Identifying the risk factors specific to each country enables specific preventive measures to be taken.

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Author contribution

Author(s) declared to fulfill authorship criteria as devised by ICMJE and approved the final version. Authorship declaration form indicating individual contribution, submitted by the author(s), is available with the editorial office.

Consent to publication statement

Author(s) declared taking informed written consent for the publication of clinical photographs/material (if any used), from the legal guardian of the patient with an understanding that every effort will be made to conceal the identity of the patient, however it cannot be guaranteed.

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Conflict of interest

The authors declare that there are no conflicts of interest.

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