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Research Article

Contribution Factors on Congenital Malformations in Neonates in Iran

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Abstract

Background: Congenital malformations are one of the most important and common types of anomalies in infants, and they are considered as the leading causes of disability and mortality in children. These malformations impose enormous costs on families and organizations involved in the treatment, maintenance, and education of patients.

Objectives: This study aimed to investigate the risk factors affecting the incidence of congenital anomalies in infants born in Iran.

Methods: In this retrospective descriptive-analytical study, we registered various information of all newborns examined and their mothers, including gender, family relationship of parents, type of delivery, types of congenital malformations, anomalies of the hands and feet, and anomalies of the nervous and reproductive systems in the maternity wards of hospitals in Iran. Data were gathered using a checklist. The relationships between different factors were assessed by chi-square test, and the factors influencing congenital malformations were investigated by logistic regression using SPSS-26 software. The significance level of all tests was 0.05.

Results: According to the results, 7.5% of newborns had congenital malformations. Eclampsia and diabetes mellitus increased the risk of congenital malformations by 15 and 11%, respectively. The risk of congenital malformations in rural areas was 12% higher than in urban areas. Factors such as consanguineous marriages, history of abortion, and gender also affected the risk of congenital malformations.

Conclusions: Necessary measures and plans in the field of premarital counseling, regular pre-pregnancy and post-pregnancy tests and controls, especially in rural and deprived areas, are essential and effective in reducing the incidence of congenital malformations.

Keywords: Contribution Factor, Congenital Malformation, Neonatal, Iran

1. Background

Congenital malformations are structural or functional anomalies at birth that lead to physical, mental, and developmental disabilities (1, 2). Genetic and environmental factors, as well as a combination of them, may cause congenital malformations. Appropriate diagnostic and therapeutic tools have gradually improved over the past decades and helped us to identify better and reduce the long-term effects and mortality. Early identification of congenital malformations is the first step to providing useful genetic counseling for parents. Nowadays, due to the importance of life expectancy in newborns, congenital malformations are the most crucial issue in health care (3). Annually, an average of 3 - 6% of newborns, about 8 million babies worldwide, are born with a severe congenital malformation, and estimates show that more than 90% of these babies are born in low- and average-income countries (4). Congenital malformations can occur as a defect or a combination of defects (5). Research showed that about 65 - 75% of congenital malformations are multifactorial. According to the results of several studies, factors such as defects in one or more genes (6), hereditary factors (7), diabetes mellitus (8-10), mother's age (11), mother's living environment during pregnancy (12), and consanguineous marriage (13-15) are the influencing factors for congenital malformations.

In a retrospective study by Verma et al. (1991) conducted on 10,000 babies born between January 1983 and March 1989, the prevalence of congenital malformations was reported as 6.6%. In this study, most of the anomalies were due to central nervous system (CNS). Anomalies were similar in both genders, although genital anomalies were more common in boys (16). Some chronic diseases like diabetes mellitus and high blood pressure in mothers are known as risk factors for many congenital malformations

(17, 18).

2. Objectives

This study aimed to examine the factors affecting the birth of infants with congenital malformations using logistic regression.

3. Methods

3.1. Patient Population

We conducted this study based on the data of neonatal malformations registered in Iranian Maternal and Neonatal Network (IMAN). In this retrospective descriptive-analytical study, we analyzed the information of all live births and their mothers in 2015 in maternity hospitals of Iran in terms of variables such as gender, birth weight of the baby, consanguineous marriage, location of residence, chronic and underlying maternal diseases, and type of delivery. The study was approved by the Ethical Committee of Tabriz University of Medical Sciences (IR.TBZMED.REC.1399.688).

3.2. Data Collection

In this study, the information was analyzed based on all severe congenital malformations, including hands, feet, and nervous system malformations, gastrointestinal disorders, and genital malformations. Data gathering was performed using a checklist.

3.3. Statistical Analyses

Data analysis was done using chi-square test to investigate the associations between different factors and factors affecting congenital malformations. Logistic regression has been used by SPSS-26 software. P-value < 0.05 was considered as statistically significant.

4. Results

4.1. Descriptive Statistics

Out of a total of 1,491,883 newborns and their mothers, 111,211 (7.5%) babies were born with congenital malformations. Most of these infants had one or two anomalies (83.77% had one malformation, and 10.80% had two malformations). Also, 768,782 (51.6%) infants were male and 722,416 (48.4%) were female. Table 1 shows the information about newborns and their mothers.

The following tables show the associations between the variables of chronic blood pressure, eclampsia, diabetes, gender, history of abortion, and place of residence of parents with a malformation based on the chi-square test. As can be seen in Tables 2 to 8, all the variables had a significant relationship with congenital malformations, except chronic blood pressure (P-value < 0.05).

Table 1. Distribution of Quality Characteristics of Mothers [a]

Variable	No. (%)
Chronic blood pressure	
Yes	16076 (1.1)
No	1475807 (98.9)
Eclampsia	
Yes	22330 (1.5)
No	1469553 (98.5)
Diabetes mellitus	
Yes	39152 (2.6)
No	1452731 (97.4)
Consanguineous marriage	
Yes	1175211 (78.8)
No	316672 (21.2)
Place of residence	
Rural	371006 (24.9)
Urban	1120877 (75.1)
History of abortion	
Yes	255240 (17.1)
No	1236643 (82.9)

[a] Diabetes variables include all mothers with type 1 diabetes and type 2 diabetes.

4.2. Logistic Regression

After examining the relationship between independent variables and dependent variables (congenital malformations), eclampsia, diabetes mellitus, consanguineous marriages, place of residence, gender, and history of abortion entered the logistic regression model (Table 9).

We analyzed the cause of birth anomalies by logistic regression analysis as the dependent variable, and the variables of eclampsia, diabetes mellitus, consanguineous marriage, place of residence, gender, and history of abortion were predictive (independent) variables. A total number of 1,491,883 neonates entered the analysis, and the full model was significant ($\chi^2 = 456.250$, df = 7, P-value < 0.001). The results showed that the variables of eclampsia, diabetes, consanguineous marriage, place of residence, infant's gender, and history of abortion significantly predicted the infants' congenital malformations. The chance of having a baby with congenital malformation was 15%

Table 2. Congenital Malformation and Chronic Blood Pressure Cross-tab

	Chronic Blood Pressure, Count (%)		Test Results		
	No	Yes	χ^2	df	P-Value
Congenital malformation			0.970	1	0.325
No	1365827 (98.9)	14845 (1.1)			
Yes	109980 (98.9)	1231 (1.1)			

Table 3. Congenital Malformation and Eclampsia Cross-tab

	Eclampsia, Count (%)		Test Results		
	No	Yes	χ^2	df	P-Value
Congenital malformation			37.151	1	< 0.001
No	1360244 (98.5)	20428 (1.5)			
Yes	109309 (98.3)	1902 (1.7)			

Table 4. Congenital Malformation and Diabetes Cross-tab

	Diabetes Mellitus, Count (%)		Test Results		
	No	Yes	χ^2	df	P-Value
Congenital malformation			48.309	1	< 0.001
No	1344795 (97.4)	35877 (2.6)			
Yes	107936 (97.1)	3275 (2.9)			

Table 5. Congenital Malformation and Abortion History Cross-tab

	Abortion history, Count (%)		Test Results		
	No	Yes	χ^2	df	P-Value
Congenital malformation			69.666	1	< 0.001
No	1145467 (83.0)	235205 (17.0)			
Yes	91176 (82.0)	20035 (18.0)			

Table 6. Congenital Malformation and Consanguineous Marriage Cross-tab

	Consanguineous Marriage, Count (%)		Test Results		
	No	Yes	χ^2	df	P-Value
Congenital malformation			85.780	1	< 0.001
No	1088821 (78.9)	291851 (21.1)			
Yes	86390 (77.7)	24821 (22.3)			

Table 7. Congenital Malformation and Place of Residence Cross-tab

	Place of Residence, Count (%)		Test Results		
	Urban	Rural	χ^2	df	P-Value
Congenital malformation			202.698	1	< 0.001
No	345324 (25.0)	1035348 (75.0)			
Yes	25682 (23.1)	85529 (76.9)			

Table 8. Congenital Malformation and Gender Cross-tab

	Gender, Count (%)		Test Results		
	Boy	Girl	χ^2	df	P-Value
Congenital malformation			13.304	1	< 0.001
No	710999(51.5)	669251 (48.5)			
Yes	57783 (52.1)	53165 (47.9)			

Table 9. Logistic Regression Analysis for Determining the Effect of Essential Factors on Congenital Neonatal Malformations

Variables and Levels	Coefficient	Standard Error	P-Value	Odds Ratio	95% CI for Odds Ratio
Intercept	-2.649	0.008	0.000	0.07	-
Eclampsia					
No	Reference	-	-	-	-
Yes	0.138	0.024	0.000	1.15	(1.095, 1.204)
Diabetes mellitus					
No	Reference	-	-	-	-
Yes	0.106	0.019	0.000	1.11	(1.072, 1.153)
Abortion history					
No	Reference	-	-	-	-
Yes	0.061	0.008	0.000	1.06	(1.046, 1.080)
Consanguineous marriage					
No	Reference	-	-	-	-
Yes	0.078	0.008	0.000	1.08	(1.066, 1.098)
Habitat					
Urban	Reference	-	-	-	-
Rural	0.111	0.007	0.000	1.12	(1.101, 1.133)
Gender					
Female	Reference	-	-	-	-
Male	0.022	0.006	0.000	1.02	(1.010, 1.035)

higher in mothers with eclampsia than in healthy mothers, and 11% higher in mothers with diabetes mellitus than in healthy mothers. Also, the chance of having a baby with congenital malformations in rural areas was 12% higher than in urban areas. A history of abortion, consanguineous marriage, and the infant's gender were factors influencing the onset of congenital malformations, although the odds ratios (OR) for these variables were close to 1.

5. Discussion

There are several influencing factors for congenital malformations, including chronic maternal illnesses such as diabetes mellitus, eclampsia, a history of abortion, and consanguineous marriages. These factors increase the chance of congenital malformations in babies. Moreover, in rural areas, the rate of congenital malformations was higher than urban areas. This may be due to the lack of facilities, regular tests, and ultrasounds, which indicates more serious attention for planning services of premarital counseling, testing, controls, and health services during pregnancy in rural areas. Also, male infants were more likely to have congenital malformations than female ones. In a study by Verma et al., maternal factors such as previous abortions, drug abuse, fever in the first trimester of pregnancy, diabetes mellitus, eclampsia, and anti-drip bleeding had a significant association with congenital malformations in infants. Our study showed a significant association between factors such as diabetes mellitus, eclampsia, and previous maternal abortions with congenital malformations in infants, which is consistent with the results of the study by Verma et al. In the study conducted by Verma et al., the malformations were similar in both genders, but in our study male infants had more malformations (16). In a multicenter case-control study in 2008, Correa et al. used data from approximately 18,000 deliveries from October 1997 to December 2003. In their study, there was a strong association between diabetes mellitus and congenital malformation, which is in line with our study results (17). In a 2012 cross-sectional study, Lin et al. concluded that the prevalence of congenital malformation in urban areas was higher than in rural areas, which is inconsistent with the results of our study (19). Kar et al. (2018), in a non-interventional hospital-based clinical trial study gathered data from September 2015 to August 2016 to analyze the prevalence of congenital malformation and the factors affecting it. They concluded that one of the factors influencing the incidence of congenital malformations is living in rural places, which is consistent with the results of our study (20). In a 2016 study in northern Iran, Kaviani et al. concluded that congenital malformations were significantly related to consanguineous marriages, which was similar to our study (21).

In a 2016 review study, Ng et al. found that consanguineous marriages may increase the chance of getting congenital malformation (22). Also, in a cross-sectional study conducted on 138 married couples and their children in 2016 by Al-Joborae et al., the prevalence of congenital malformations was significantly higher for parents with relatives (especially close relatives such as cousins) than the stranger parents (23). The results of these studies are similar to those obtained in the present study.

Lary et al. studied the prevalence of congenital malformations and concluded that male infants were more at risk for congenital malformations than females, which is in line with our study (24). In a 2014 descriptive-analytical study, Amini Nasab et al. examined the data of 118 infants from 2007 to 2011. Their results showed that congenital malformation was more common in male infants (55.9%) than in females (44.1%) (25). These results are also similar to our results.

Although chronic blood pressure is one of the most important and influential factors in the birth of babies with congenital malformations (18, 26, 27), we did not witness the effect of this factor in our study. Bellizzi et al. (2016) analyzed data from the World Health Organization (WHO) multi-country survey in which they reported 310,401 babies from 359 centers in 29 countries. They used logistic regression model with a random effect for detecting associations between six widespread congenital malformations and four high blood pressure disorders in mothers in the form of chronic blood pressure, preeclampsia, eclampsia, and chronic hypertention. This study showed that high blood pressure in mothers significantly increased the risk of congenital malformations of the kidneys, limbs, and lips/cleft/palate (18).

5.1. Conclusions

Our findings suggest that such measures as premarital counseling, regular pre-pregnancy and post-pregnancy tests, and controls, especially in rural and deprived areas, are essential to reduce the incidence of congenital malformations in Iran.

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Footnotes

Authors' Contribution: Study concept and design, Sevda Riyahifar and Kayvan Mirnia; Analysis and interpretation of data, Sevda Riyahifar and Reza Ali Akbari Khoei; Drafting of the manuscript, Sevda Riyahifar; Critical revision of the manuscript for important intellectual content, Reza Akbari Khoei, Kayvan Mirnia, and Sevda Riyahifar; Statistical analysis, Sevda Riyahifar.

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