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Risk Factors for Congenital Malformations among Population in the Agadir Region at Morocco

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Abstract. A prospective case-control study at the regional level was conducted in the pediatrics and neonatology department of Hassan II hospital in Agadir in Morocco from April 2016 to April 2018. In this study, we aimed to study congenital anomalies in the population of the study region regarding the frequency and highlight the associated risk factors. The types of congenital malformations have been classified according to the International Classification of Diseases (ICD-10). Univariate analyzes were performed to identify the variables associated with the etiology of the malformations. Multiple logistic regression was used to characterize the associations between the MC, and the determining explanatory variables are taken into account simultaneously. The results found that congenital disabilities were significantly associated with the consanguinity level of the child, the prematurity of childbirth, the family history of CMs, the Body Mass index. (BMI) of the mother and the presence of a significant trauma during pregnancy. Our results have made it possible to highlight the existence of an association between a certain number of risk factors and the occurrence of congenital malformations.

Keywords: congenital malformations, risk factors, Morocco.

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INTRODUCTION

World Health Organization (WHO) reported that approximately 76,000 newborn babies die each year before 28 days from congenital disabilities (1). These anomalies result from a pathological process during embryonic development, following a genetic (intrinsic) predisposition or the exposure of an extrinsic risk factor or a combination of both (1, 2). The prevalence of major CMs is around 3% of live births (3,4). Global surveys have shown that the majority of congenital disabilities vary considerably from country to country. A wide variation in this prevalence is observed worldwide and ranges from less than 1% to more than 8%. Congenital disabilities are structural, functional, including metabolic disorders, present at birth. The etiology of congenital disabilities is multifactorial, determined by a large number of genetic and environmental factors. The risk factors for the majority of congenital disabilities are unfortunately unknown.

Only a few studies exist in Morocco concerning the association between congenital anomalies and the various risk factors. This work contributes to a better understanding of these risk factors involved in the etiology of congenital anomalies in Morocco and the region concerned by the study. To explore the relationships between CMs and possible risk factors, univariate analysis was used to identify the variables associated with the etiology of congenital malformations. Then we subjected the data to multiple logistic regression to characterize the associations between congenital malformations, and the determining explanatory variables are taken into account simultaneously. Using logistic regression for multivariate analysis has improved the accuracy of risk factor estimates by adjusting for other associated variables by reducing the effect of confounders.

OBJECTIVE

This study aims to establish the epidemiological profile of the major congenital malformations and the contribution to the exploration of the significant risk factors for the population of the region of Agadir in Morocco.

MATERIAL AND METHODS

This is a case-control study carried out in the pediatrics and neonatology department of Hassan II hospital in Agadir. The study population comprises 3701 newborns admitted to the neonatology service from April 2016 to April 2018. For each newborn, a questionnaire is filled out, including information relating to economic, biological, and social factors, including maternal experience, socioeconomic level, the presence of inbreeding, the course of pregnancy and childbirth, as well as neonatal data.

The factors analyzed are as follows: Sex (1= male, 2=femelle) , Maternal age (1= MA :≤35) , 2 = MA : >35)), Multiparity (1= yes, 2= non), Prematurity (1= yes, 2= non), Twin pregnancy (1=yes, 2= non), Birth weight (1=BW <2,5kg, 2= 2,5kg≤BW≤4kg, 3=BW >4kg), Pregnancy monitoring (1 = not follow-up, 2 = poorly follow-up, 3 = well follow-up), Interval between pregnancies (1 = IBP <18 months, 2 = 18≤ IBP ≤59, 3= IBP > 59 months), Family history of CMs (1=yes, 2= non), Consanguinity (Child) (1= yes, 2= non), Consanguinity (Mother) (1= yes, 2= non), Socio-economic level (1= low, 2= medium, 3= high), Education level (1= low, 2= medium, 3= high), Infectious diseases (1= yes, 2= non), Chronic diseases (1= yes, 2= non), Body Mass Index (1=IMC <18.5, 2=18,5≤IMC≤24,9, 3=25≤IMC≤29,9 and 4=IMC≥30), Presence of significant trauma during pregnancy (1= yes, 2= non).

The types of congenital disabilities have been classified according to the International Classification of Diseases (ICD-10) codes (5). The diagnosis of congenital anomalies is based on the clinical evaluation of the newborn by the pediatrician and other appropriate investigation methods such as radiography, ultrasound, echocardiography, etc. Univariate and multivariate logistic regression analyzes were performed to verify the association between congenital malformation and the various risk factors. Raw odds ratios were obtained for all variables. The uni-varied analysis allowed us to select the explanatory variables which are sufficiently strongly linked to the occurrence of congenital malformations.

The descending step-by-step procedure performed multivariate logistic regression. It consists of all the previously selected variables (variables with a p-value <0.20) and gradually removing those that do not provide sufficient information to the model allowing an adjustment of the calculated Odds Ratio (adjusted OR). The confidence interval (CI) of OR is calculated by: exp $^{(\text{CI de}}$ (with CI of β : $\hat{\beta} \pm Z_{1-\alpha/2} SE_{\hat{\beta}}$). The statistical analyzes were carried out using SAS software version 9.4 (6) and SPSS version 24.0 for Windows (7).

RESULTS

Between April 2016 and April 2018, 115 cases with congenital malformations were detected among newborn children during the study period. The types of congenital disabilities have been classified according to the International Classification of Diseases (ICD-10) codes. The systems involved in decreasing order in some cases observed were: osteoarticular system and muscle abnormalities (34 cases), digestive system abnormalities (9 cases), circulatory system abnormalities (10 cases), cleft lip and cleft palate (16 cases), urogenital system abnormalities (10 cases), multiple and skin malformations (9 cases) and chromosomal abnormalities (6 cases).

Table 1 shows that among infants, 50.3% were males, and 49.7% were females. Concerning the Socioeconomic level of the family, Low level constituted 35.6% of the sample. The medium level constituted 62.3%, and the high level only 2.1 %. The examination of the educational level of the father of the family shows that more than 90% of fathers of families have a low or medium level of education (92.1%), and only 7.9% have a high level (bachelor's degree and above) (Table 1).

Table 1: Demographic characteristics of newborns admitted to the Hassan II Hospital, Agadir, Morocco, between April 2016 and April 2018.

Characteristics		Frequency	Percent (%)
Sex	Male	1861	50.3
	Female	1840	49.7
Socioeconomic level (family)	Low	1298	35.6
	Medium	2273	62.3
	High	75	2.1
Education level (father)	Low	1566	43
	Medium	1710	49.2
	High	287	7.9

The results of the uni-varied analysis are set out in Table 2. Among the risk factors studied, a very highly significant link with the occurrence of congenital malformations is observed for maternal age (p <0.001, OR: 4.98, 95% CI: 3.13 - 7.94), the mother's body mass index (BMI) (p = 0.0044, OR: 1.89, 95% CI: 1.22 - 2.93), the family history of CMs (p <0.001 , OR: 6.16, 95% CI: 3.18 - 11.92), the consanguinity level of the child (p <0.001, OR: 3.08, 95% CI: 1.92 - 4.94), the trauma during pregnancy (p <0.001, OR: 3.74, 95% CI: 2.57 - 5.45).

Table 2: Results of the Univariate Analysis.

	n	OR	95% CI	p-value
Sex ratio	3701	1.59	0.99 - 2.54	0.0584
Maternal age	3696	4.98	3.13 - 7.94	<0.0001
Multiparity	3696	1.91	1.12 - 3.26	0.0169
Prematurity	3698	0.15	0.02 - 1.08	0.0098
Twin pregnancy	3694	3.15	1.02 - 9.74	0.0458
Birth weight	3701	1.40	0.60 - 3.36	0.4569
Pregnancy monitoring	3694	1.20	0.67 - 2.12	0.5407
Interval between pregnancies	3694	1.60	0.98 - 2.61	0.0603
Family history of CMs	3694	6.16	3.18 - 11.92	< 0.0001
Consanguinity (Child)	3696	3.08	1.92 - 4.94	<0.0001
Consanguinity (Mother)	3696	1.27	0.76 - 2.13	0.3600
Socioeconomic level	3664	1.76	1.11 - 2.80	0.0162
Education level	3664	2.05	1.21 - 3.49	0.0078
Infectious diseases	3666	0.73	0.46 - 1.17	0.1920
Chronic diseases	3664	1.29	0.70 - 2.40	0.4138
BMI (Body Mass Index)	3694	1.89	1.22 - 2.93	0.0044
Trauma	**3664**	3.74	2.57 - 5.45	< 0.0001

OR: Odds Ratio, 95% CI: 95% confidence intervals (CI) of OR.

The results of the multivariate analysis are given in Table 3. Among the risk factors studied, a very highly significant link with the occurrence of congenital malformations is observed for the consanguinity level of the child (p <0.001 , ORa: 2.30, 95% CI: 2.13 - 2.48), the presence of CMs in family (Family history of CMs) (p <0.001, ORa: 2.14, 95% CI: 1.98 - 2.32), trauma during pregnancy (p <0.001, ORa : 1.46, 95% CI: 1.35 - 1.57), the consanguinity level of the mother (p = 0.0024, ORa: 1.23, 95% CI: 1.14 - 1.33) and prematurity (p = 0.0063, ORa: 1.13, 95% CI: 1.05 - 1.22). Significant associations are observed with maternal age (p-value: 0.0362) and body mass index (p-value: 0.0222)

Table 3: Results of stepwise logistic regression analysis.

	B	ORa	CI inf.	CI sup.	p-value
Sex ratio	0.077	1.08	1.00	1.17	0.0469
Maternal age	0.101	1.11	1.02	1.20	0.0362
Prematurity	0.123	1.13	1.05	1.22	0.0063
Family history of CMs	0.726	2.14	1.98	2.32	< 0.000
Consanguinity (Child)	0.832	2.30	2.13	2.48	< 0.000
Consanguinity (Mother)	0.207	1.23	1.14	1.33	0.0024
BMI (Body Mass Index)	0.113	1.12	1.03	1.21	0.0222
Trauma	0.376	1.46	1.35	1.57	< 0.000

B: Coefficient B, ORa: Adjusted odds ratio, CI: 95% confidence intervals

DISCUSSION

The univariate and multivariate analysis results made it possible to highlight a significant role of maternal age and the body mass index. Several studies have shown that the mother's advanced age beyond 25 is associated with an increased risk of congenital disabilities in the fetus (8,9). Several authors report overweight and obesity (high BMI) as risk factors for congenital anomalies [10]. Obesity before pregnancy is associated with a wide range of unwanted pregnancies, including congenital disabilities such as neural tube defects and congenital heart disease (11, 12, 13, 14).

Our study also shows that consanguinity is very highly associated with the onset of birth defects. Several authors have reported the level of consanguinity as a risk factor for congenital anomalies [15, 16, 17]. Inbreeding was highest among birth defects, and relatives were more likely to have infants with multiple malformations (15). Shieh et al., Have shown that congenital heart disease is more frequent in consanguineous unions in the study population, mainly when the coefficient of kinship is greater than or equal to 0.0625 (16).

The prevalence of congenital anomalies has been observed mainly in consanguineous marriages compared to non-consanguineous marriages (17).

In a medium or high degree of consanguinity population, the formulation of a public health program with a multi-approach strategy. It included education on the genetic consequences of consanguineous marriages, prenatal diagnosis, neonatal screening, and genetic counseling, which is necessary to avoid an excessively high prevalence of congenital anomalies (18).

This study found that trauma experienced during pregnancy is one of the main factors linked to the increased prevalence of birth defects. The use and analysis of data from a population-based case-control study explore the relationship between certain life events during the preconception period. Several types of congenital anomalies have shown that the experience of " at least one stressful event during the preconception period was associated with an increased prevalence of childbirth in infants with birth defects. This study suggests that women who experience stressful events during conception or early gestation may be at increased risk for giving birth to infants with certain birth defects (19). Other authors have reported that the frequency of malformations is higher in pregnancies exposed to severe life events than in those without exposure (20). Different results highlighted the importance of maternal traumatic experience and its potential long-term influence on mother-child interaction behavior (21).

It is found that prematurity is among the factors that increase the risk of birth defects. Several studies have shown that prematurity is associated with a considerably increased risk of birth defects in the fetus (22, 23, 24). Congenital anomalies are associated with a high rate of neonatal morbidity for premature births. These associations can be explained by a higher rate of pregnancy complications and constitute an independent risk factor for neonatal morbidity and perinatal mortality (25).

The essential risk factors were highlighted in this study: CMs in the family (Family history of CMs). The risk of having a family member affected is significantly increased in the presence of family history. Similar observations have been made in other studies (26, 27). Family aggregation of a few birth defects suggests genetic, and other specific risk factors in recurrent birth defects and supports a vital genetic component (26, 27).

CONCLUSION

Our study showed that inbreeding, prematurity, body mass index, presence of deformities in siblings, and trauma suffered during pregnancy are the main factors linked to the increased prevalence of congenital anomalies and the risk of neonatal and infant mortality. To be complete and precise, we must compare the number of birth defects registered in the birth register or the hospital register with the number collected in the national birth defects register. High-quality and high-quality population studies are needed to confirm these associations and for many other groups of congenital anomalies.

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