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Chapter

Consanguinity Marriage Increases Risk of Newborn's Congenital Anomalies in Sulaimani City

Niaz Mustafa Kamal

Abstract

Consanguineous marriage may cause the transfer of two recessive defective mechanisms, one from the mother and the other from the father, to offspring, which may cause the appearance of congenital anomalies. This study is aimed at determining the role of consanguineous marriage with congenital anomalies and their types in Sulaimani City. This is a retrospective case-control study based on hospital records. The study was conducted in Maternity Teaching Hospital of Sulaimani City from January 1 to December 31 of 2018. A record of 522 neonates (260 newborns with CA and 262 newborns with the absence of CA) were delivered from the Maternity Teaching Hospital and all private hospitals which were collected from the statistic section of the maternal and child care unit of the Preventive Health Department. The sample of neonates without congenital anomalies was collected randomly from hospital records, and stillbirth was excluded. Categorical variables were summarized as frequencies and percentages, while for numeric variables mean and the standard deviation were used. Chi-square test was applied to compare categorical variables and odds ratios using STATA 12. A p value less than 0.05 was considered statistically significant if p smaller than 0.001 was reported as < 0.001. The mean age of the newborn children with CA was (1.79, SD 2.04) and for the mother's cases was (29.59, SD 4.97). The commonest type of CA was congenital heart disease (25%); low birth weight and gender were statistically associated with types of CA (χ^2 = 30.53 and p = 0.006 vs. χ^2 = 45.3, p = <0.000, respectively). There was a significant correlation between parental marriage with anomalies (OR, 1.83, p = 0.001) and increase mothers age 30 years and over (OR, 2.56, p = 0.03). For eliminating this problem, there is an urgent need for educating unmarried people on the deleterious effects of consanguineous marriage, especially in Sulaimani City with high overall consanguinity rates.

Keywords: consanguinity, congenital anomalies, spina bifida, Sulaimani, neonates

1. Introduction

Birth defects, congenital abnormalities, and congenital anomalies (CAs) are interchangeable terms used to describe developmental defects that are present at birth and can be defined as structural or functional anomalies, including metabolic disorders, which are present at the time of birth [1]. Birth defects are various groups of disorders of prenatal origin that can be caused by single gene defects, chromosomal disorders, multifactorial inheritance, environmental teratogens, and

micronutrient deficiencies. Maternal infections such as rubella, maternal illnesses like diabetes mellitus (DM), iodine and folic acid deficiency, exposure to medicinal and recreational drugs including alcohol and tobacco, certain environmental chemicals, and doses of radiation are all other factors that cause birth defects [2]. Birth defects are encountered frequently by pediatricians and regarded as an important cause of childhood morbidity and mortality. Birth defects can be classified according to their severity and pathogenic mechanism or whether they are involving a single system or multiple systems [3]. Structural anomalies are considered overt when they are visible on inspection; otherwise, they are considered "occult" [4].

Congenital malformation (CM) began to emerge as one of the major childhood health problems, and it refers to any abnormality, whether genetic or not, which is present at birth. Treatment and rehabilitation of children with CM are costly, and complete recovery is usually impossible [5].

The etiology of CM is genetic (30–40%) and environmental (5–10%). Among the genetic etiology, chromosomal abnormality constitutes 6%, single gene disorders 25%, and multifactorial 20–30%; however, for nearly 50% of CM, the cause is yet to be known [6]. The pattern and prevalence of congenital anomalies may vary over time or with geographical location, thereby reflecting a complex interaction of known and unknown genetic and environmental factors including sociocultural, racial, and ethnic variables [7].

Consanguineous marriage is referred to a marital union among close biological kin. In clinical genetics, it is called the relationship by marriage between first and second cousins [8, 9]. Consanguineous marriage is most common in the Middle East and among Islamic populations. The rate of consanguineous marriage in different countries is dependent on different factors like education level, religion, local tradition, and socioeconomic status [9]. Studies over several decades have shown that there is a high correlation between consanguineous marriage and inherited congenital malformation [10]. There are many risk factors increment to the prevalence of congenital malformations; however, the consanguineous marriage remains the risk factor contributing to congenital anomalies [11]. The current study was conducted to determine if there is a correlation between parental consanguinity and the appearance of congenital anomalies in Sulaimani City.

2. Methodology

This is a retrospective case-control study based on hospital records. The study was conducted in Maternity Teaching Hospital of Sulaimani City from January 1 to December 31 of 2018. A record of 522 neonates (260 newborns with congenital anomalies and 262 newborns without congenital anomalies) were delivered from the Maternity Teaching Hospital and all private hospitals which were collected from the statistic section of the maternal and child care unit of the Preventive Health Department. The Ph.D. is the main body responsible for preventive health services and collection of public health-related data from all hospital and health-care centers of the city. The sample of neonates without congenital anomalies was collected randomly from hospital records. The study excluded stillbirth. The recorded data included demographic data and neonatal and maternal data. The parental consanguinity data were obtained from the hospital records which were recorded as first and second relatives. The study was approved by the ethics committee of the Technical College of Health, and permission was also taken from the Preventive Health Department.

The type of birth defects was classified by the diagnostic standardization of CM from the ICD-10 system [12]. Records of neonates with multiple congenital

anomalies were grouped depending on whether those anomalies qualified as a specific syndrome or not. The diagnosis was made by a pediatrician examining the neonate immediately or within a few days of delivery. If they qualified as a specific syndrome, they were then categorized into that syndrome. If no syndrome could be classified, then the anomaly is referred to the system affected and by the specific anomaly. When more than two systems were involved, it was recorded as multiple congenital anomalies. Birth weights ≥2.5 kg was considered to be normal weight, while birth weight <2.5 kg as low birth weight. Categorical variables were summarized as frequencies and percentages, while for numeric variables mean and the standard deviation were used if normally distributed variables. The chi-square test is used for determining the association between categorical variables. Odds ratio and adjusted odds ratio were calculated to determine risk factors, and p value equal and less than 0.05 was considered statistically significant. Smaller p values were reported as <0.001 if they were smaller than 0.00.

3. Results

The study included 522 neonates (260 neonates with CA and 262 neonates without CA). 51.5% of the neonates with CA was male and 48.5% was female. Of the 54.6% of CA neonates from inside the city and 62.2 of non-CA neonates from

Characters	**Congenital anomalies n=(260)**	**None congenital anomalies n=(262)**	χ^2	p **value**
Sex			0.007	0.9
Male	134 (51.5%)	136 (51.9%)		
female	126 (48.5%)	126 (48.1%)		
Residence			3.1	0.08
Inside Sulaimani	142 (54.6%)	163 (62.2%)		
Outside Sulaimani	118 (45.9%)	99 (37.8%)		
Mothers occupation			1.3	0.3
Employed	222 (85.4%)	214 (81.7%)		
None employed	38 (14.6%)	48 (18.3%)		
Mother's age				
<25	10 (3.9%)	13 (5.1%)	40.43	<0.0001
26-29	100 (39.4%)	167 (66%)		
≥30	144 (56.7%)	73 (28.9%)		
Parental consanguinity			6.7	0.01
Yes	58 (22.1%)	35 (13.5)		
No	204 (77.9%)	225 (86.5%)		
Birth weight			0.38	0.5
Low birth weight g < 2500	161 (62.2%)	169 (64.8%)		
Normal birth weight g> 2500	98 (37.8%)	92 (35.2%)		

Table 1.
Comparison of Socio-demographic characteristic of congenital and none congenital anomalies.

Category	Mean case	Mean controls	*p* value
Child age/days	1.79 (2.04)	2.58 (5.86)	0.04
Mothers age/years	29.59 (4.97)	32.13 (5.32)	<0.0001

Table 2.
Mean age distribution of the mothers and neonates.

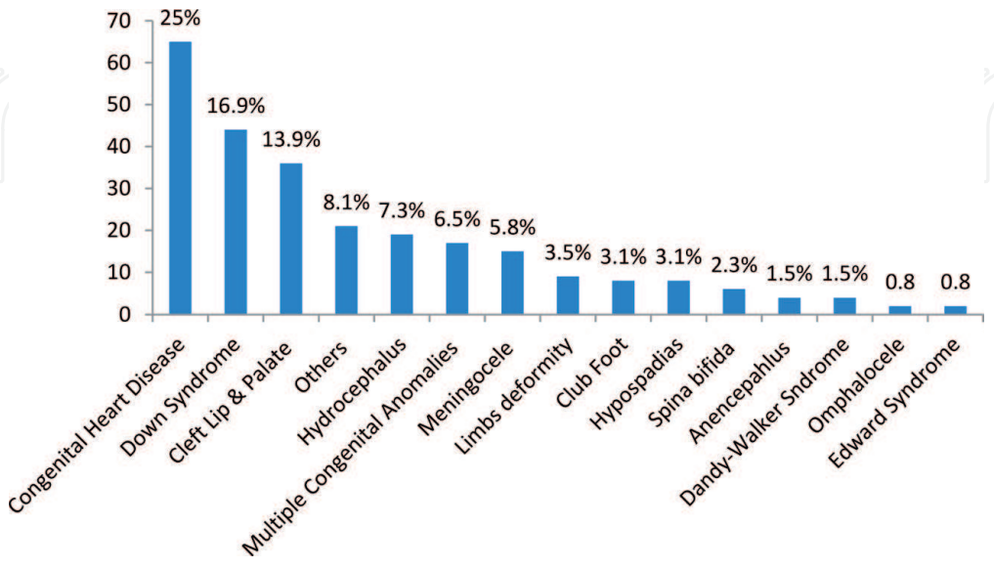

Figure 1.
Distribution types of congenital anomalies.

outside the city, 85.4 and 81.7% of mothers for two groups are employed, while the rest (14.6 and 18.3%) were not employed. Mothers have children with CA aged below 25 was (3.9%), 26–29 years was (39.4%) and those aged 30 and over was (56.7%), while mothers have children without CA aged 25 and below was (5.1%), 26–29 years was (66%) and those aged 30 and over (28.9%). This difference was statistically significant in the p = <0.0001. The consanguineous marriage of mother's neonates with CA and with the absence of CA was (22.1 vs. 13.5%), respectively, this difference was sadistically significant p = 0.01. There was a slight difference between the birth weight of CA and none a neonate which was presented in the **Table 1**.

The mean age of the newborn children with CA was 1.79, SD 2.04, and for the newborn without CA was 2.58, SD 5.86, with p = 0.04. The mean age of the mother's cases was (29.59, SD 4.97) and the mother's controls were (32.13, SD 5.3) with p = <0.0001 (**Table 2**).

Figure 1 shows the distribution types of congenital anomalies; the commonest type of CA was congenital heart disease (25%), followed by Down syndrome (16.9%) and left lip and plate (13.9%), while the less common types were omphalocele and Edwards syndrome (0.8%), respectively.

The gender and birth weight (low birth weight < 2.5 kg) are compared with each type of congenital anomalies. There is a statistically significant association between gender and birth weight with the types of congenital anomalies (**Table 3**). Congenital heart disease was common in male (61.5%) than female (38.5%), left lip and palate (66.7%) in male compared to female (33.3%), and Down syndrome (52.3%) in male higher than female (47.3%), while others, MCA and club foot, were higher among female than male. This difference was statistically significant with χ^2 = 30.53 and p = 0.006. Low birth weight was statistically associated with types of

Congenital anomalies	Neonate gender		Low birth weight < 2.5 kg
	Male	Female	
Congenital heart disease	40 (61.5%)	25 (38.5%)	35 (53.9%)
Omphalocele	2 (100%)	0 (0%)	2 (100%)
Cleft lip and palate	24 (66.7%)	12 (33.3%)	31 (86.1%)
Hydrocephalus	9 (47.4%)	10 (52.6%)	13 (68.4%)
Multiple congenital anomalies	4 (23.5%)	13 (76.5%)	2 (12.5%)
Meningocele	4 (26.7%)	11 (73.3%)	8 (53.3%)
Limb deformity	4 (44.4%)	5 (55.6%)	5 (55.6%)
Club foot	2 (25%)	6 (75%)	6 (75%)
Hypospadias	8 (100%)	0 (0%)	6 (75%)
Spina bifida	2 (33.3%)	4 (66.7%)	3 (50%)
Anencephalus	2 (50%)	2 (50%)	2 (50%)
Dandy-Walker syndrome	2 (50%)	2 (50%)	0 (0%)
Down syndrome	23 (52.3%)	21 (47.3%)	28 (63.6%)
Edwards syndrome	1 (50%)	1 (50%)	1 (50%)
Others	7 (33.3%)	14 (66.7%)	19 (90.5%)
Total	**n = 260 (100%)**		**n = 161 (62.2%)**
Statistical analysis	**$\chi 2 = 30.53, p = 0.006$**		**$\chi 2 = 45.3, p = <0.0001$**

Table 3.
Different congenital anomalies by gender and child birth weight of any congenital anomalies.

Congenital anomalies	Mother's age	Parental consanguinity
	30 years and over	
Congenital heart disease	20 (31.8%)	9 (13.9%)
Omphalocele	0 (0%)	0 (0%)
Cleft lip and palate	9 (25%)	6 (16.7%)
Hydrocephalus	5 (26.3%)	4 (21.1%)
Multiple congenital anomalies	6 (35.3%)	2 (11.8%)
Meningocele	5 (35.7%)	2 (13.3%)
Limb deformity	3 (33.3%)	1 (11%)
Club foot	2 (28.6%)	1 (12.5%)
Hypospadias	1 (12.5%)	1 (12.5%)
Spina bifida	0 (0%)	0 (0%)
Anencephalus	1 (33.3%)	1 (25%)
Dandy-Walker syndrome	2 (50%)	1 (25%)
Down syndrome	13 (30.9%)	5 (11.4%)
Edward syndrome	0 (0%)	0 (0%)

Congenital anomalies	Mother's age	Parental consanguinity
	30 years and over	
Others	6 (28.6%)	2 (9.5%)
Total	**n = 135 (28.8%)**	**n = 35 (13.5%)**
Statistical analysis	**$\chi 2 = 30.1, p = 0.3$**	**$\chi 2 = 4.3, p = 0.1$**

Table 4.
Different congenital anomalies by mother's age and parental consanguinity of any congenital anomalies.

Risk factors	Occurrence of congenital anomalies					
	OR (95% CI)	Chi square	*p*-value	AOR (95% CI)	Chi square	*p*-value
Consanguineous marriage						
No	Reference			Reference		
Yes	1.83 (1.1–2.9)	6.7	0.001	1.42 (0.9–2.3)	2.04	0.2
Mother's age						
<25	Reference			Reference		
26–29	0.78 (0.3–1.8)	0.33	0.6	0.8 (0.3–2.0)	0.2	0.7
≥30	2.56 (1.7–6.2)	4.7	0.03	2.6 (1.1–6.5)	4.9	0.03

Table 5.
Factors associated with the occurrence of congenital anomalies.

CA with $\chi^2 = 45.3$ and $p = <0.000$. CHD was 53.9%, cleft lip and palate 86.1%, Down syndrome 63.6%, and others and hydrocephalus 90.5 vs. 68.4%, respectively.

We analyzed the type of congenital anomalies with the mother's age (30 years over) and parental consanguinity. Overall, 28.8% of the anomalies were to mothers aged 30 years and over, 13.5% of the anomalies from consanguineous marriage. It's found there was no association between two factors and type of congenital anomalies (**Table 4**).

To found the parental consanguinity was confounder risk factors for increased the risk of congenital anomalies the odds and adjusted odds ratio was calculated **Table 5**. Consanguineous marriage will have a greater risk of having children with CA, (odds 1.83, CI 1.1–2.9, χ^2, 6.7, and $P = 0.001$). Increasing age of the mothers 30 years and over also increases the risk of congenital anomalies (odds 2.56, CI 1.7–6.2, χ^2, 4.7, $\boldsymbol{p} = 0.03$). When we adjusted consanguinity with the mother's age, it remains a risk factor for those mothers aged 30 and over for increasing the chance of CA (AOR 2.6, CI, 1.1–6.5, χ^2, 4.9, $p = 0.03$).

4. Discussion

The current study aimed to identify the association between parental consanguinity and congenital malformations and their types in the Maternity Teaching Hospital in Sulaimani City. The most common birth defects were congenital heart diseases, Down syndrome, and cleft lip and palate. They were presented in 25, 16.9, and 13.9% out of 260 congenital anomalies, respectively. Is similar to the studies done in Sulaimani [13, 14] and also is contrary to the study was done in Saudi Arabia [15]. The study demonstrated a highly significant difference between

the birth weight of newborn (low birth weight < 2500 kg) with different types of congenital anomalies with $p = 0.006$. Is corresponding with the population study was performed in Centers for Disease Control, Atlanta and the case–control study done in Sulaimani, Iraq [13, 16] and also gender showed that there is a significant difference with types of congenital anomalies which is in accordance with the study done in Neliti and the United State [11, 17], while is in contrary with the studies done in Sulaimani and Iran [13, 18]. When we analyzed parental consanguinity with the patterns of anomalies, we found there is no correlation between these factors with types of CA. These findings are consistent with the study on the prevalence of congenital malformations in consanguineous and non-consanguineous marriages [19], and also the study was done in India [20]. In addition, when we analyzed the rise of maternal age > 30 years with types of congenital malformations, we found no difference in this factor with the occurrence of congenital anomalies. Our finding is in contrary to a retrospective study in Latvia [21]. Our study represented consanguineous marriages that play a major role in the occurrence of congenital malformations compared with non-consanguineous marriage (odds 1.83), and when we adjusted consanguinity with maternal age, it remains a significant risk factor. The results are in agreement with the study [19] and the study done in Saudi Arabia [22]. Our finding shows no increased risk of advanced maternal age with congenital anomalies which is not in agreement with the study of the United States [23]. The current study has some limitations which should be considered before making extrapolation. The major limitation of this study was a retrospective case–control study based on data derived from passive sources of the hospital records. It is therefore likely that the study missed some data and congenital anomalies that do not present early in life, such as heart defects, pyloric stenosis, and anomalies of the urinary system, which could also explain the low level of defects found compared with other studies.

5. Conclusion

In conclusion, congenital anomalies were mostly observed among consanguineous marriage compared with non-consanguineous marriage. It is highly recommended that consanguineous marriages be prevented especially if the previous consanguinity is present in the family. Premarital counseling, especially on the subject of parental consanguinity, is advised.

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