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Birth Defects and Parental Consanguinity in the North of Iran

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Authors' contributions

This work was carried out in collaboration between all authors. Authors NK and MS managed the literature searches, wrote the protocol, managed the study process and wrote the first draft of the manuscript. Author EG managed the literature searches and wrote the first draft of the manuscript. Author MA performed analyses of the study. Author MJG designed the study, wrote the protocol, managed the study process and wrote the first draft of the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Aim: Consanguineous marriages are considered as a risk factor of some congenital anomalies. This study was done to determine the relationship between birth defects and consanguineous marriage in northern Iran.
Methodology and Study Design: This hospital based study with consecutive sampling was performed on 1545 live newborns with birth defects in Golestan province, northern Iran during 2007–2012. Consanguinity of parents of each newborn was recorded.
Results: From 1545 malformed newborn who born during the study period, 480(31.06%) of newborns were born to consanguineous parents. 395(82.3%) of parents were first cousins followed by second cousins 85(17.7%). The number of 557 congenital malformations was detected in 480

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malformed newborns were born from consanguineous parents. The percent of congenital anomalies in newborns were born from consanguineous vs. non-consanguineous parents were as following; heart anomalies (45.2% vs. 51.2%), followed by anomalies of central nervous system (17.5% vs. 15.5%), limb anomalies (22.9% vs. 14.8%), urogenital anomalies (7.1% vs. 5%) and gastrointestinal anomalies (23.3% vs. 18.4%). There was a significant association between the percentage of heart, limb and gastrointestinal anomalies with Consanguinity of parents ($P<0.05$).

Conclusion: This study showed that the congenital anomalies was significantly related with consanguineous marriages in north of Iran.

Keywords: Birth defects; consanguinity; heart anomalies; central nervous system anomalies; Iran.

1. INTRODUCTION

Parental consanguinity is a risk factor for many adverse health outcomes because it favors the emergence of genetic based diseases in the offspring [1,2]. Consanguinity is defined as the marriage between individuals who have common ancestor. Inheriting identical copies of a mutant allele occurs in many autosomal recessive disorders, particularly in circumstances of consanguinity which is detrimental to health [3].

Consanguineous marriage (inbreeding) has been reported as an important factor in the appearance of autosomal recessive diseases and congenital anomalies, including hydrocephalus, postaxial hand polydactyly and bilateral cleft lip cleft palate, bipolar disorders, depression, infant mortality, child deaths, spontaneous abortions and stillbirths [4,5].

The detrimental health effects associated with consanguinity are caused by the expression of rare, recessive genes inherited from common ancestor(s). In general terms, inbreeding is associated with loss of biological fitness [6].

Congenital malformations are structural abnormalities that due to defective embryogenesis or abnormal development. Newborns of consanguineous parents are at two-times greater risk than newborns of non-related parent's for autosomal recessive disorders [7].

The etiology of CM includes genetic (30-40%) and environmental (5 to 10%), however, for nearly 50% of CM is unknown. Among the genetic etiology, chromosomal abnormality constitutes 6%; single gene disorders 25% and multifactorial 20-30% [8].

The less common a disorder, the greater is the influence of consanguinity on its prevalence, a generalization that applies to recessive multi genes disorders as well as to single gene conditions [9]. For this reason, many previously unrecognized genetic diseases have first been diagnosed in highly endogenous communities and in significant portions of cases the underlying mutation may be unique to the community, these community specific patterns of disease leads to major problems when attempting to estimate the burden imposed by consanguinity associated mortality at national or at regional levels [8].

Consanguinity ratios in different parts of Iran ranged from 30 to 85% [10]. In another country, such as the province of Antalya, Turkey; there has been a significant increase in the rate of consanguineous marriages, approximately 40.7% between populations. The most frequent type of marriage was between first cousins [11].

In the Arab communities, interfamilial unions currently account for 20-50% of all marriages. First-cousin unions are especially popular and constitute almost one quarter of all marriages in many Arab countries. Consequently, autosomal recessive (AR) dysmorphic syndromes constitute a considerable proportion of all birth defects among Arabs populations [12].

The twofold increase in the proportion of children with birth defects among first-cousin parents in the Pakistani population was reported [13].

In the Middle East, Iran is one of countries with an elevated grade (38.6%) of inbreeding [14]. Also, in Iran Georgian consanguineous marriages have been reported to be up to 23.3% [15].

In our country, the rate of consanguineous marriages is high, therefore, it can be considered as one of the most important reasons behind the genetic disorders, birth defects and the infants' inabilities [14].

Several studies in the other part of Iran were reported the high prevalence of consanguineous

marriage in the population. But there is no documented report in this regard in our province. Therefore, this study was design in this region for the first time.

This study was done to determine to the patterns of congenital malformations in the newborns and the association of malformations with consanguinity of parents in Golestan province, north of Iran.

2. SUBJECTS AND METHODS

This hospital based study with consecutive sampling was performed on 1545 malformed newborns in 13 hospitals in Golestan province, north of Iran during 5 years period from March 2007 to March 2012. Ethical approval for the study was obtained from the ethics committee of Golestan University of Medical Sciences. The mothers consent was obtained for the study, along with a clearance from the Institutional ethical committee.

Golestan Province is located in the north of the country, south of the Sea with 1.7 million population and 20,380 km² area.

All newborns who had been delivered in the hospital during study period were examined and screened for congenital malformations by pediatricians. For each birth we recorded the following sex, maternal age, habitat, consanguinity of parents and type of congenital malformations.

The type of birth defects was classified by the diagnostic standardization of congenital malformations from the international classification of disease (ICD-10) codes. It should be noted that in this study, type of congenital heart defects has been detected by echocardiography procedure. Also cleft palate and cleft lip with or without cleft palate are classified in the congenital digestive disorders categories.

Consanguineous marriage was classified by the degree of relationship between couples.

Consanguinity was defined as three groups: first-cousin marriages (children of parent), other consanguinity (half first and second-degree cousins, distant consanguineous Marriages, if known) and non-consanguineous marriages [16]. The data was analyzed using SPSS version 16. The rates of malformed newborns and malformations were compared using statistical T-test and the Chi-square tests. The level of significance was determined at $p<0.05$.

3. RESULTS

Out of 1545 malformed newborn who born during the study period, 480(31.06%) of newborns were born from consanguineous parents. Among whom 254(53%) were males, 220(45.8%) females and 6(1.2%) with ambiguous genitalia. There was no significant difference between gender of newborns and consanguineous marriage.

395(82.3%) of consanguineous marriages were first cousins followed by second cousins with 85(17.7%).

Consanguineous marriages were detected in 263 (54.8%) of rural and 217(45.2%) of urban mothers. There was statistical difference between the rate of residency of parents and consanguineous marriage (P<0.001) (Table 1).

In this study, The number of 557 congenital malformations were detected in 480 malformed newborns were born from consanguineous parents. The percent of congenital anomalies in newborns were born from consanguineous vs. non-consanguineous parents were as following; heart anomalies (45.2% vs. 51.2%), followed by anomalies of central nervous system (17.5% vs. 15.5%), limb anomalies (22.9% vs. 14.8%), urogenital anomalies (7.1% vs. 5%) and gastrointestinal anomalies (23.3% vs. 18.4%). There was a significant association between the percent of heart anomalies, limb anomalies and gastrointestinal anomalies with consanguineous marriage of parents (P<0.05). The prevalence of congenital malformations in consanguineous marriages is depicted in Table 2.

4. DISCUSSION

In this study, 31.06% of malformed newborns were born from consanguineous parents. Our finding is higher than Yüksel study in Turkey with 28.4% [16] and lower than Kanaan study in Lebanon with 42% [6].

Our results showed a significant association between consanguinity and congenital malformations which is agreement with the findings of Yüksel study [16] which found a significant association between spontaneous abortions, infant deaths and genetic disorder in children with consanguineous marriages.

Table 1. Sex, residency and mother age in consanguineous parents in north of Iran

	Consanguinity		
	Yes (%)	**No (%)**	**P-value**
Sex			
Female	220(45.8)	475(44.6)	0.371
male	254(53)	585(54.9)	
ambiguous genitalia	6(1.2)	5(0.5)	
Residency			
Rural	263(54.8)	470(44.1)	0.001
Urban	217(45.2)	595(55.9)	
Mother age			
18 ≥	32(6.7)	47(4.4)	0.1
19-35	423(88.1)	946(88.8)	
≥ 36	25(5.2)	72(6.8)	

Table 2. The percentage of type of congenital malformations in newborns with and without consanguineous marriage

	Consanguinity		
	Yes (%)	**No (%)**	**P-value**
Heart anomalies			
Yes (%)	217(45.2)	545(51.2)	0.03
No (%)	263(54.8)	520(48.8)	
Central nervous system anomalies			
Yes (%)	84(17.5)	165(15.5)	0.32
No (%)	396(82.5)	900(84.5)	
LIMB anomalies			
Yes (%)	110(22.9)	158(14.8)	0.001
No (%)	370(77.1)	907(85.2)	
Urogenital anomalies			
Yes (%)	34(7.1)	53(5)	0.09
No (%)	446(92.9)	1012(95)	
Gastrointestinal anomalies			
Yes (%)	112(23.3)	196(18.4)	0.02
No (%)	368(76.7)	869(81.6)	

Also, a study in Ahvaz in south of Iran [17] reported a significant association between mental disabilities, blindness, deafness and Physical disabilities with consanguineous marriages. Several studies in other region of Iran including Isfahan [18], Kashan [19], Mashhad [20] and Yazd [21] have reported that consanguinity significantly associated with an increase of congenital malformations.

The prevalence of different congenital malformations in neonates varies from one country to another, which might be due to racial and environmental factors or differences in survey methods.

A study In Pakistan has shown that the rate of births defects, still births and neonatal deaths were common in the newborns of consanguineous parents [7].

In this study, newborns from first cousin marriages had the risk of CHD in compared to those born to unrelated parents.

Also, in a study in Pakistan [7], 21% of parents with malformed newborns were consanguineous marriages. In the population studies in North-Eastern France [22] consanguineous mating was known in 1.21% of the cases with congenital anomalies in comparison with 0.27% in controls (P<0.001).

Out of 480 malformed newborns were delivered to consanguineous parents, 53%, 45.8% and 1.2% were males, females and ambiguous genitalia, respectively. In Mosayebi study in Kashan, central part of Iran [19] congenital malformations was more common in the males (male to female ratio 2.1:1).

Our result is similar to shih et al. [23], the two studies in Iraq [24,25] and India [26]. Also, a study in Riyadh [27] was reported that parents' consanguinity effects on the pattern of congenital heart defects.

In our study, Limb anomalies were significantly associated with consanguineous marriages. This finding is supported by Sahin et al. [28] study in Turkey and Sreenivas et al. [3] in India regarding congenital talipes equinovarus.

Also, we found significant association between oral clefting and consanguinity. This finding is agreement with other reports [29,30]. Alamoudi study in Jeddah [29] and Ravichandran study [30] in Riyadh in Saudi Arabia were found a relationship between consanguinity and cleft palate and cleft lip with or without cleft palate.

In this study, the commonest form of consanguinity among parents was found in the first cousin followed by second cousin. Our finding is similar to shahri finding in Ahvaz, a city in southwest of Iran [17] and Mosayebi and Movahedian study in Kashan a city in central of Iran [19]. Mosayebi and Movahedian study [19] reported that malformations in the consanguineous group were significantly more common in offspring of first-cousin marriages than second-cousin or more distant relative marriages.

Indeed, Sandridge et al. [31] reported that sizeable proportion of the participants did not know that a more distant cousin marriage theoretically could be a less genetically risky choice to potential offspring than a closer cousin marriage.

In other hand, Mehrabi et al. [32] showed that although the consanguinity for malformed patients was high, but there was no significant relationship between malformation and the degree of relation of the parents.

In India, the most common form of consanguineous marriage in all major societies was first cousin, which is strongly influenced by traditions. The unions like the marriage to mother's brother's daughter is the strongly preferred form of consanguineous union among South Indian Hindus [33]. Also, in South Asian Muslim communities first-cousin union, i.e. to father's brother's daughter, to father's sister's daughter, to mother's brother's daughter, and to mother's sister daughter, are arranged [34].

According to our results, the authors recommend that all offspring of consanguineous marriages should be thoroughly examined for birth defects. Also, premarital counseling on the subject of parental consanguinity is recommended.

Based on previous studies, some factors such as amount of folic acid and maternal zinc in blood are effective upon the occurrence of congenital malformations [35,36].

5. CONCLUSIONS

Congenital anomalies were significantly related with consanguineous marriages and the first cousins was the common form of consanguineous marriage in north of Iran.

6. LIMITATION

This study was done only on Live birth newborns and still birth not enrolled in our study.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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