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The Frequency of Consanguinity and Its Related Factors in Parents of Children with Genetic Disorders

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ABSTRACT

Background & Objective: Consanguinity increases the incidence of genetic disorders. The frequency of consanguinity varies in different societies. There was no data regarding the frequency of consanguinity in Zanjan province. This study aimed to describe the prevalence of consanguineous unions in the parents of children with genetic disorders and its related factors in Zanjan, Iran.

Materials & Methods: This cross-sectional study included children with genetic diseases referring to the medical genetics clinic in Zanjan's Musavi Hospital during 2014-2018. Data including consanguineous unions in families (up to three previous generations), types of genetic illnesses, child and parents' age, parental educational level, and occupation were collected and analyzed using descriptive statistics, independent t-test, and chi-square test.

Results: Of the 87 children, 41 (47.7%) were male, and 50 (59.5%) resided in urban areas. The mean age of the children was 6.5 years. The educational level of 56.6% of fathers and 50.6% of mothers were highschool diploma or higher. The parents of 44 children (51.8%) had consanguineous unions. The most common type of consanguineous union was between first cousins. The nature of the genetic disorders in 63 (72.4%) of children was molecular. The proportion of consanguinity was significantly higher in parents of children with molecular than chromosomal disorder (P<0.0001). Consanguinity had also a significant relationship with the children's age (P=0.04).

Conclusion: This study's outcomes illustrate that parents of more than half of children with genetic disorders had consanguinity and the frequency of consanguinity was more common in parents of children with molecular disease than chromosomal disorder. Given that, it is necessary to avoid consanguineous marriage as much as possible, and families with a history of molecular genetic disease, should be informed of the possible consequences.

Keywords: Consanguinity, Genetic disorders, Children

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Introduction

Genetic disorders are instigators of mortality and morbidity and produce a burden of medical expenses. Consanguinity increases the incidence of genetic disorders. The main underlying factor is the inheritance of autosomal recessive genes derived from a common ancestor. Genetic disorders are also likely to be related to the parents' familial relationship; a closer relationship increases the likelihood of inheriting defective genes. For example, it is estimated that about 12.5% (one-eighth) of genes are shared in first cousins. Therefore, an average of 6.25% of their children's genes will be homozygote, and in this case, to be more precise, autozygote, meaning that some areas of their genome will acquire similar genes from their parents (1).

About 20% of the world's population resides in areas with a tendency for consanguinity, and around 8.5% of all children result from consanguineous unions. Consanguineous unions are widespread in Africa and Asia, especially in Islamic countries, while being less prevalent in Western countries. The justification of continued consanguineous unions may be due to a tendency to conserve the family bloodline or the various social, economic, and cultural advantages of consanguineous unions (especially between first cousins). In Egypt, many people believe that interfamilial unions causes higher compatibility between couples and is less likely to result in divorce (2-5).

The prevalence of consanguineous unions in the Middle East varies and is usually influenced by religious, racial, ethnic, and socioeconomic factors, such as the norms accepted for consanguineous unions (6-9). Among Arab countries, consanguineous unions' prevalence varies from

33% in Morocco (10) to 68% in Egypt (11). In a study in Saudi Arabia, the prevalence of consanguineous unions was 51.3%, and there was a significant association between the level of education and consanguineous unions; the proportion of consanguineous unions was 63% in the illiterate and those with primary education and 46% in higher levels of education (12). The prevalence of consanguineous unions in Iran has yet to be determined. According to a study by Taybi et al., between 1195 infants in Yazd, the prevalence of consanguineous unions was 25% (13). A study by Mokhtari et al. showed that 44% of infants with congenital malformations (born in Tehran) were the result of consanguineous unions (14).

Since the frequency of consanguineous unions differs between societies and cultures and is influenced by religious, racial, and ethnic factors, and considering that no study has been performed regarding the prevalence of consanguinity in Zanjan, northwest of Iran, we decided to study the frequency of consanguineous unions in the parents of children with genetic disorders and identify the associated factors.

Materials and Methods

This cross-sectional study was accomplished by total sampling that involves the entire population of 87 couples who had children with genetic disorders and were referred to the medical genetics clinic in Zanjan's Musavi Hospital between 2014 and 2018. Information on the age of the children and their parents, parental education level, parental occupation, types of genetic illnesses, consanguineous unions in parents, and their families (up to three previous generations) was collected. The Ethical Committee approved the Zanjan University of Medical Sciences study (Ethical code: IR.ZUMS.REC.1397.271), and informed consent was obtained from all subjects.

The Kolmogorov-Smirnov test was employed to evaluate the distribution of quantitative variables. Values were expressed as numbers (percentages) and mean ± standard deviation, as appropriate. Comparisons were performed by the chi-square test for categorical, independent t-test for normally distributed, and Mann–Whitney test for non-normally distributed variables. Statistical analyses were performed using SPSS version 16.0 for Windows (SPSS, Chicago, IL, USA). P< 0.05 was considered statistically significant.

Results

The demographic and clinical information of the children and their parents is presented in Table 1. In a group of 87 children with genetic diseases, 41 were male (47.7%), and 50 (59.5%) were born in a city. Most of the children's mothers and fathers had a diploma or higher education (50.6% and 56.6%, respectively). Most of the children's fathers were self-employed (33.1%), while 95.2% of mothers were homemakers (Table 1).

The parents of 30 children (35.3%) had a third-degree family relationship (first cousins), 14 children (16.5%) had a distant (fourth or fifth degree) family relationship (first cousins once removed), and parents of 41 children (48.2%) had no family relationship. There were 52 children (63.4%) with a history of consanguineous unions in the family (up to three generations ago) (Table 1).

The genetic disorder of 63 children (72.4%) was of molecular origin, and the rest were chromosomal (Table 1). Among molecular conditions, the highest frequency was related to deafness, consisting of 7 people (11.1%), then epidermolysis bullosa, ichthyosis, Duchenne, and SMA (4 people each) (6.3%) and three people (4.8%) in the category of metabolic diseases. Among chromosomal conditions, the highest prevalence was related to trisomy 21 (Down syndrome) in 10 people (41.7%), then having an extra Y chromosome, and Triple X syndrome in 2 people in each group (8.3%).

Among children with molecular genetic disorders, the parents of 39 had (63.9%) consanguineous unions, while in children with chromosomal genetic disorders, five parents (20.8%) had consanguineous unions (P <0.0001, table 1). Consanguinity frequency distribution did not show a statistically significant difference in other variables, including gender, residence, education, and parents' occupation, consanguineous unions in genealogy (Table 1).

Table 1. Frequency distribution of consanguinity by study variables

Variables	Total n (%)	Consanguineous n (%)	Non-consanguineous n (%)	P value
Sex				
Male	41 (47.7)	21 (47.7)	23 (52.3)	0.37
Female	45 (52.3)	23 (57.5)	17 (42.5)	
Residential area				
Urban	50 (59.5)	22 (44.0)	28 (56.0)	0.06
Rural	34 (40.5)	22 (64.7)	12 (35.3)	
Education of father				
Illiterate/Primary	18 (21.7)	10 (55.6)	8 (44.4)	0.89

Variables	Total n (%)	Consanguineous n (%)	Non-consanguineous n (%)	P value
Secondary	18 (21.7)	10 (55.6)	8 (44.4)	
Diploma	30 (36.1)	15 (51.7)	14 (48.3)	
Higher	17 (20.5)	7 (43.8)	9 (56.3)	
Education of mother				
Illiterate/Primary	24 (28.9)	15 (62.5)	9 (37.5)	
Secondary	17 (20.5)	7 (41.2)	10 (58.8)	0.38
Diploma and higher	42 (50.6)	20 (50.0)	20 (50.0)	
Occupation of father				
Employee	22 (26.5)	8 (38.1)	13 (61.9)	
Manual worker	10 (12.0)	8 (80.0)	2 (20.0)	0.11
Self-employed	26 (31.3)	11 (44.0)	14 (56.0)	
Farmer	25 (30.1)	15 (60.0)	10 (40.0)	
Occupation of mother				
Housewife	79 (95.2)	41 (53.2)	36 (46.8)	0.35
Employed	4 (4.8)	1 (25.0)	3 (75.0)	
Consanguinity in generations				
Yes	52 (63.4)	13 (43.3)	17 (56.7)	0.28
No	30 (36.6)	29 (55.8)	23 (44.2)	
Type of genetic disease				
Molecular	63 (72.4)	39 (63.9)	22 (36.1)	<0.001
Chromosomal	24 (27.6)	5 (20.8)	19 (79.2)	

The mean age of the referred children's mother and father was 31.3 and 35.9 years, respectively, and the mean age of the children was 6.5 years (Table 2). The mean age of children with consanguineous unions was higher than children whose parents did not have consanguineous unions (P = 0.04, Table 2). The mean age of the parents in both groups, with and without consanguineous unions, was not significantly different.

Table 2. The association of consanguinity with the age of children and their parents.

Variables	Total Mean±SD	Consanguineous Mean±SD	Non-consanguineous Mean±SD	P-value
Age	6.5± 5.2	7.5± 5.2	5.2± 5.1	0.04
Age of father	35.9± 7.6	34.9± 6.5	37.1± 8.5	0.33
Age of mother	31.3± 6.9	30.7± 6.2	31.9± 7.7	0.70

Discussion

In this study, the frequency of consanguineous unions of parents of children with genetic diseases referred to the genetic clinic of Ayatollah Mousavi Hospital in Zanjan in the years 2014 to 2018 was 51.8% (35.3% with close family relations and 16.5% with distant family relations), which indicates a high proportion of consanguinity in this region. A study conducted in Pakistan in 2018 on pregnant women reported a first cousin's union frequency of 48.9% **(15)**. In Iran, studies such as ours studying the frequency of consanguineous unions of parents of children with suspected and diagnosed genetic diseases have reported high rates of consanguineous unions (Hafizi et al. 79.7%, Rabieian et al. 69.8% and Shahri et al. 61.2%

(16-18). A study on Lebanese couples showed 42% of first cousins' union (19). In the study of Atai et al., Which was performed on clients in premarital counseling centers in Kohgiluyeh and Boyer-Ahmad Provinces, the consanguineous union ratio was 43.4% (20). In the study of movafagh et al., the consanguineous union rate in patients referred to the Welfare Genetics Center and Qazvin University of Medical Sciences was 38.6% (21).

Haji Esfandiari et al. also reported that 30.4% of parents of special education children had consanguineous unions. Other Iranian studies on the parents of healthy children or the general population have reported a few familial union incidences (the study of Movahedian 21.8%, Rashid Shamali et al. 15.3% and davati et al. 17.7%) (22-24). As these studies show, consanguineous unions' frequency varies due to geographical, cultural, and ethnic differences. The prevalence of consanguineous unions in our study is closer to the results of other studies of parents of children with suspected genetic disorders.

Our study results showed that the proportion of first-degree consanguineous unions (first cousins) to distant family relation is more than doubled (35.3% versus 16.5%). In Hafizi et al.'s study, the ratio of third-degree consanguineous unions and consanguineous unions in the fourth degree in parents of children with motor disabilities referred to the Quds Rehabilitation Center in Mashhad was 79.7% and 13.6%, respectively (16). In Rabieian et al. on children referred to the genetics clinic in Imam Khomeini hospital in Tehran, the proportion of third-degree consanguineous unions is 69.8%, and consanguineous unions in fourth, fifth, and of distant families was 23.8% (17). In the study of Shahri et al., third-degree family unions and unions with distant relatives were observed in 61.2% and 23.8% of parents of special education children, respectively (18). These studies' results are consistent with our study that in children with disabilities, first or third-degree family unions (first cousins) are far more common than familial unions in the fourth, fifth, or distant family. Therefore, this clarifies the role and importance of first-degree consanguineous unions (first cousins) in the development of the disease due to having a higher percentage of similar genes than consanguineous unions in the fourth, fifth, or distant family.

In our study of close consanguineous unions, the highest frequency was related to the marriage of first cousins, with relations being from the maternal side (40%). This finding was also observed in the study by Rabieian et al. (17). In this study, the frequency of third-degree consanguineous unions with maternal origin was 45.3%. The authors attributed the high prevalence of consanguineous unions with maternal family members to the level of mothers' emotional reliance on their families, which led to their children's bonding. The same is true of the results of our study.

In this study, the association between consanguineous unions and variables such as age, sex, residence, type of disease, age of parents, education, and occupation of parents was also examined. The proportion of consanguineous unions in the parents of children with a molecular genetic disorder was significantly higher than the proportion of consanguineous unions in the parents of children with a genetic disease of the chromosomal kind. Rabieian et al. also observed in their study that the majority of conditions in the children of parents without family relationships were with dominant autosomal and chromosomal patterns that were not related to consanguineous unions (17).

In the present study, consanguineous marriage was not associated with parental age. In the study of Davati et al., the couple's age was not related to consanguineous marriage (24). However, in our study, consanguineous unions were significantly associated with the child's age. The average age of children whose parents were related was less than children whose parents were related. Although this finding seems plausible because chromosomal abnormalities are more common in children whose parents have no family relationship and, like chromosomal trisomies, are usually diagnosed at a younger age, the interpretation of this finding in our study should be more cautious because for most children in this study, the age at the time of referral was recorded, which may be different from the age of onset of the disease.

In our study, there was no relationship between consanguineous marriage and parental education. This is consistent with the findings of other studies of Davati et al. (24) and the study of Rashid Shomali et al (23) and inconsistent with the results of a study by Omrani et al. (25). Failure to see such a relationship in our study could be due to the low number of fathers (17 people) and mothers (5 people) with a university education, which did not correctly perform this comparison.

One limitation of our study was missing data, which was solved in almost all cases with present contact information.

Conclusion

The present study results showed that the frequency of consanguineous unions of parents of children with genetic diseases referred to as the genetic clinic of Ayatollah Mousavi Hospital in Zanjan was high, and more than two-thirds were first-cousin marriages. Also, the proportion of consanguineous unions in parents of children with a molecular genetic disorder was significantly higher than the parents of children with chromosomal genetic disorders. Given that molecular genetic diseases are mostly autosomal recessive and are mainly seen in consanguineous marriages, Therefore, it is necessary to avoid consanguineous marriage as much as possible, and in areas and families

with a history of molecular genetic disease, the public should be informed of the possible consequences.

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Conflict of Interest

The Authors declare that they have no conflict of interest.

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