Clinical outcomes of consanguineous marriages in Turkey

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Turkey has a high rate of consanguineous marriages. Different nationwide surveys indicate that today 20-25% of marriages are consanguineous, with the rate having increased over the last 15 years. The results of many studies show that the rate of consanguinity among parents of children with rare recessive diseases is quite above Turkey's average and that the high consanguinity rate is one of the underlying factors of high infant and child mortality and fertility in Turkey.

Key words: autosomal recessive disease, consanquinity, fertility, infant mortality.

Turkey has a high rate of consanguineous marriage, indicating a strong preference for this form of union. Turkey's Demographic and Health Surveys reflect the trend in this respect since 1968[1-5]. In 1968, the rate of consanguinity between couples was around 30%. Fifteen years later (1983) it was 20%, and then the rate began to increase again at that point, reaching 25% 15 years later (Table I).

Table I. Distribution (%) of Consanguineous Marriages in Turkey by Region

Region	1968*	1983*	1988*	1993*	1998*
West	16.6	10.1	12.8	13.7	16.3
South	38.0	29.4	29.6	28.6	29.9
Center	29.1	22.4	20.8	25.6	27.4
North	26.0	21.7	23.3	22.1	24.2
East	37.8	32.9	30.8	34.4	39.2
Turkey	29.2	20.9	21.1	23.0	25.1

* Turkey's Demographic and Health Surveys.

The aim of this paper was to show the relation between consanguinity and infant mortality and the frequency of parental consanguinity in some autosomal recessive diseases in Turkey. Due to the biological effects of human inbreeding, consanguineous marriages, which are widely practiced in Turkey, may be considered as one of the important variables explaining high infant mortality through autosomal recessive diseases.

The impact of consanguineous marriages on mortality and fertility was analyzed from the 1988 Turkish Population and Health Survey[6]. The sample was a nationally representative probability sample of households, and the consanguinity rate was 21.1% in this survey. The pattern observed in consanguineous marriages indicated traditional behavior, mostly practiced among people of low socioeconomic level. However, when two important variables affecting infant mortality, education level and size of settlement place, were controlled in urban areas where living conditions are better than in rural areas, the difference in infant mortality due to first-cousin marriages was clearly observed. In rural areas this differential was not so apparent, possibly due to the concentration of many other adverse factors affecting infant mortality[6].

In the above-mentioned study, total marital fertility rates, mean number of total pregnancies, children even born and living children were found significantly high for women in first-cousin marriages. The study results showed that couples with first-degree consanguinity have high fertility as compared to those in nonconsanguineous unions. Therefore, consanguineous marriages may also be considered as one of the factors underlying the high total fertility in Turkey[6].

The high mortality rates in consanguineous families can be explained by the deleterious effects of recessive genes. In fact, in many autosomal recessive disorders, consanguinity between parents is much higher than seen in the general population.

Patients admitted to the Department of Genetics of Hacettepe University Children's Hospital were analyzed to determine the relationship

between consanguinity and recessive disorders. Among the parents of the patients diagnosed with a recessive disease, consanguinity was 75.5%. For multifactorial disorders this figure was 34.9% and for autosomal dominant, X-linked, chromosomal and sporadic disorders 22.7%.

Various studies in Turkey revealed that parental consanguinity in autosomal recessive disease shows a spectrum from 100 percent to near Turkey's average rate of consanguinity (Table II). The highest figures belong to propionic acidemia (100%) and Friedreich's ataxia (96.4%) and the lowest figure belongs to familial Mediterranean fever (FMF), which is one of the common autosomal recessive diseases in Turkey. The carrier frequency of FMF was calculated as 1:12 and parental consanguinity was determined as 28.7% in a study comprised of 610 patients with FMF[27].

Table II. Parental Consanguinity Rate in Various Diseases in Turkey

Disease	Consanguinity rate (%)	References
Organic aciduria	70.4	15
Propionic acidemia	100.0	7
Methylmalonic acidemia	87.5	7
Maple syrup urine disease	84.0	7
Friedreich's ataxia	96.4	8
Limb-girdle muscular dystrophy	90.0	9
Bloom's syndrome	90.0	10,11
Fanconi's aplastic anemia	78.0	12
Glycogen-storage disease type I	77.8	13
DIDMOAD syndrome	72.7	14
Laron type growth hormone insufficiency	70.0	16
Congenital muscular dystrophy	68.4	17
Congenital adrenal hyperplasia	56.4	18
Thalassemia	65.0	19
Ataxia-telangiectasia	65.0	20
Type 1 hereditary tyrosinemia	63.6	21
Phenylketonuria	59.0	22
Wilson's disease	57.3	23
Spinal muscular atrophy	57.0	24
Urea cycle enzyme defect	53.4	15
Cystic fibrosis	44.2	25
Cystinuria	37.5	26
Familial Mediterranean fever	28.7	27
Cleft lip ± cleft palate	27.0	28
Insulin-dependent diabetes mellitus	23.9	29
Cleft palate	22.0	28
Neural tube defects	20.0	30

The importance of consanguinity in various congenital malformations inherited multifactorially, such as neural tube defects and cleft lip and/or palate (CL ± CP) is relatively small. In a series with 140 patients, the frequency of parental consanguinity was 22% among CP cases and 27% in cases with CL ± CP[28]. Among 93 cases with neural tube defect followed in the Genetic Unit of Hacettepe University Children's Hospital, consanguinity was 22%[30].

Diabetes mellitus is also a multifactorially inherited chronic disease in childhood. Parental consanguinity among the patients with insulin-dependent diabetes mellitus was 23.9% which is near the average rate in Turkey[29].

All the above-mentioned studies show that when a recessive trait has a high frequency in a population, such as FMF in Turkey, the rate of consanguinity is not very high, whereas in diseases in which the carrier frequency is low, the consanguinity rate among parents of children with such diseases, such as some metabolic and neurologic disorders, is high. However, even in the diseases with high carrier frequency such as cystic fibrosis, phenylketonuria and thalassemia, the parental consanguinity rate is quite above Turkey's average. This shows that a high consanguinity rate together with a high gene frequency is responsible for the high incidence of these autosomal recessive diseases in Turkey.

In conclusion, the high consanguinity rate in Turkey causes the high incidence of many autosomal recessive disorders and is one of the underlying factors of high infant and child mortality and fertility.

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