

# Consanguineous Marriage is Still a Risk Factor of Congenital Malformations in Sakarya-Turkey

## Akraba Evliliği Türkiye Sakarya Bölgesindeki Konjenital Anomalilerin Hala Önemli Bir Nedenidir

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**ABSTRACT** The purpose of this study is to provide an overview to risk factors of birth defects and to determine the general attitudes and behaviours of the pregnant women during pregnancy process in the region of Sakarya in Turkey. This is a definitive retrospective study carried out between 3rd April-2nd June 2007. The sample group of the normal child group is randomly selected from Sakarya Gynecology and Child Hospital and the sample group of the children with abnormalities is randomly selected from Canada Training and Research School in Sakarya. The data for the study was obtained by the means of the survey form prepared by the researchers. 230 families were included to the study. When we appreciate the relationship between the couples we see that 10.4% of group 1 and 30.4% of group 2 were married with relative. 4.3% of group 1 and 30.4% of group 2 were cross cousin marriage. There was a significant difference ( $p < 0.001$ ) between the two groups. The results revealed differences between the sample groups of normal and faulty birth childrens parents in terms of consanguineous and non-consanguineous matings. Such a discussion, if joined widely by first step therapy medical doctors and midwife, can result in more coordinated and effective approaches to the prevention of environmentally provoked abnormalities through beter understanding of the nature and management of risk factors result in birth defects.

**Key Words:** Consanguinity, birth defects, pregnancy

**ÖZET** Çalışma doğumsal anomalilerde risk faktörlerini gözden geçirmek ve Türkiye Sakarya bölgesindeki gebe kadınların genel alışkanlıklar ve davranış biçimlerini belirlemek için düzenlenmiştir. 3 Nisan-2 Haziran 2007 tarihleri arasında tanımlayıcı retrospektif bir çalışma olarak planlandı. Sağlıklı çocuk grubu "Sakarya Kadın Doğum ve Çocuk Hastanesi'ne" başvuran hastalardan rasgele seçilirken (Grup 1), örnek grubu yine aynı bölgedeki "Kanada Eğitim ve Araştırma Okulu'ndan" anomalili çocuklar arasından rasgele oluşturuldu (Grup 2). Çalışmadaki veriler, araştırmacılar tarafından hazırlanan inceleme formları esas alınarak elde edildi. Çalışmaya bilgilendirilmiş onam formunu imzalayan 230 aile dahil edildi. Çiftler arasındaki akrabalık ilişkisi değerlendirildiğinde bu oran 1. grupta %10.4 oranında izlenirken 2. grupta %30.4 olarak bulundu. 1. grupta %4.3 olarak izlenen 1. derece kuzen evliliği, 2. grupta %9.5 olarak belirlendi ve iki grup arasında istatistiksel olarak anlamlı ( $p < 0.001$ ) değerlendirildi. Sağlıklı ve doğumsal anomalili grup çocuklarının ebeveynleri arasında akraba evliliği olan ve olmayan grup arasında anlamlı farklar vardır. Doğumsal anomalilerde risk faktörlerini daha iyi anlayabilmek, kontrol edebilmek ve çevresel faktörlerin tetiklediği anomalileri önleyebilmek için her şeyden önce tıp hekimleri ve hemşirelerin katılımıyla birinci basamak tedavi hizmetlerinde etkili koordine bir bakış açısında olunmalıdır.

**Anahtar Kelimeler:** Kan bağı, doğumsal anomaliler, gebelik

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**B**irth defects may be defined as abnormalities of biological form and/or function resulting from abnormal/incomplete differentiation and development. 'Teratogenesis' generally is used to refer to the processes involved in development of such abnormalities. Birth defects can be classified in a number of different ways, and the use of different schemes has led to some general confusion about causes and mechanisms. The most important consequence of any approach to the general subject is clarity in our thinking about how we can prevent or modify the severity of such phenomena.<sup>1,2</sup>

Experimental teratology was never intended to supply an answer to the causes and prevention of congenital malformation. To prevent malformations, not just by the expedient of aborting malformed fetuses, it is necessary to know what the causes of congenital malformations are. The cause of congenital malformations can be divided into 3 categories: unknown, genetic, and environmental. The cause of a majority of human malformations is unknown. A significant proportion of congenital malformations is unknown (65-75%) cause is likely to have an important genetic component (15-25%). The other suspected causes are environmental (10%), maternal conditions (alcoholism, diabetes, smoking) (4%), infectious agents (3%), mechanical problems (amniotic band constrictions etc.) (2%) and at last chemicals, prescription drugs, high-dose ionizing radiation, hyperthermia (<1%).<sup>3</sup>

As mentioned previously, only a small percentage of birth defects are attributable to prescribed drugs, chemicals, and physical agents.<sup>4,5</sup> Among environmental factors, dangerous lifestyle seems to be the greatest hazard for the development of the fetal consuming alcohol and smoking tobacco. Alcohol may cause fetal alcohol syndrome or at least fetal alcohol efficacy during pregnancy but often unavoidable because approximately 50% of pregnancies are unplanned.<sup>6</sup> Recently, several studies have indicated the rate of consanguinity ranging between 20 and 70% in the Middle East. Turkey is one of the countries with a high rate of consanguineous unions in the Middle East.<sup>7</sup>

When a clinician responds to a parent's inquiry, 'What caused my child's birth defect?' the pediatrician should respond in the same scholarly manner that would be used in performing a differential diagnosis for any clinical problem. After a complete examination of the child and a review of the genetic and teratology medical literature, the clinician must decide whether the child's malformations are attributable to a genetic cause or an environmental toxin or agent. He may not be able to conclude definitively or presumptively the cause of the child's birth defects. Then this information must be conveyed to the patient in an objective and compassionate manner.<sup>8</sup>

This study was planned as a two group of randomly selected normal and children with abnormalities. The purpose of this paper is to provide an overview of birth defects and their relationship to many factors such as nicotine, alcohol, infectious disease, radiation, drugs, consanguinity and others. Such a discussion if joined widely by people training can be effective to the prevention of abnormalities.

## PATIENTS AND METHODS

This is a definitive retrospective study carried out between 3<sup>rd</sup> April- 2<sup>nd</sup> June 2007 after the approval of Internal Review Board of Staff of Sakarya Gynecology and Child Hospital and Canada Training and Research School.

### PATIENTS

The sample group of the normal child group was randomly selected from Sakarya Gynecology and Child Hospital (Group 1) and the sample group of the children with abnormalities was randomly selected from Canada Training and Research School (Group 2). Abnormalities in the group 2 were not classified but 85% of all was Down's syndrome and the others had physical and cerebral defects.

### INCLUSION CRITERIA

The families included to the study which can provide verbal consent to participate and provide sufficient information to determine the term of pregnancy and the family knowledge.

## EXCLUSION CRITERIA

Who did not accept to participate and cannot provide sufficient information.

## DATA COLLECTION

The data for the study was obtained by the means of the survey form prepared by the researchers. The preliminary application of the prepared survey form was carried out on ten families from each group. A hundred and fifteen families were included to the study from each group.

## STATISTICAL ANALYSIS

Data were analyzed by SPSS version 12.0 (SPSS Inc, Chicago, IL). Chi-square test was used to determine the differences between the groups of subjects. Differences were considered significant when P-values were less than 0.05.

## RESULTS

When we evaluated the results; in the group 1 5.2% of the women were  $\leq 20$  years old, 75.6% was 21-35 and 19.2% was up to 35 while in the group 2,  $\leq 20$  years old women were 2.6%, 21-35 were 61.8%, and

up to 35 were 35.6%. When we investigated the education level of group 1 the percentage of educated ones after primary school are 65.2% and in the group 2 71.3%. The women at work in the group 1 was 4.3% and in the group was 28.7%. The marriage age percentage of women was not significantly different between the groups. When we appreciated the relationship between the couples, we saw that %10.4 of group 1 and %30.4 of group 2 were married with relative. %4.3 of group 1 and %9.5 of group 2 were cross cousin marriage. There was a significant difference ( $p < 0.001$ ) between the two groups (Table 1).

When we appreciated the prolificacy properties of women, 1 pregnancy in group 1 was 32.2% and in group 2 was %25.2 while the  $2 \leq$  number of existing child in group 1 was 53.9% and in group 2 73.9%. One and up miscarriage in group 1 was 26.1% and in group 2 was 36.5%. There was no significant difference between the groups concerning abortion. Early birth percentage in the group 2 was higher 25.2% than the group 1 11.5% (Table 2). One and up dead birth in-group 1 was 10.4% and in group 2 was 12.4%. There was no significant difference between the groups about dead birth. When we examine the

TABLE 1: The profile of patients.

Variable	total	No. (%) of subjects		statistics
		controls	cases	
Age group:				
$\leq 20$	9 (3.9)	6(5.2)	3(2.6)	
21-35	158 (68.6)	87(75.6)	71(61.8)	
$> 35$	63 (27.5)	22(19.2)	41(35.6)	$p < 0.000$
Education level:				
University	3 (1.3)	3 (2.6)	-	
Secondary	61(26.5)	32 (27.8)	29 (25.2)	
Primary	157(68.3)	75 (65.2)	82 (71.3)	
illiterate	9(3.9)	5 (4.3)	4 (3.5)	$p > 0.314$
Work status:				
Working	15 (6.5)	5 (4.3)	10 (8.7)	
Notworking	215 (93.5)	110 (95.7)	105 (91.3)	$p > 0.624$
Age of marriage:				
$\leq 20$	121 (52.6)	62 (53.9)	59 (51.3)	
21-35	108 (47.0)	52 (45.2)	56 (48.7)	
$> 35$	1 (0.4)	1 (0.9)	-	$p > 0.674$
Kinship of husband:				
Not kinship	183 (79.6)	103 (89.6)	80 (69.6)	
Cousin	16 (7.0)	5 (4.3)	11(9.5)	
Distant relative	31 (13.5)	7 (6.1)	24 (20.9)	$p < 0.001$

**TABLE 2:** Prolificacy properties.

	No. (%) of subjects			statistics
	total	controls	cases	
<b>Number of pregnancy:</b>				
1	47 (20.4)	33 (28.6)	14 (12.2)	p < 0.012
2	83 (36.1)	41 (35.7)	42 (36.5)	
3 ≤	100 (43.5)	41 (35.7)	59 (51.3)	
<b>Existing child:</b>				
nonexistent	17 (7.4)	16 (13.9)	1 (0.9)	p < 0.001
1	66 (28.7)	37 (32.2)	29 (25.2)	
2	97 (42.2)	37 (32.2)	60 (52.2)	
3 ≤	50 (21.7)	25 (21.7)	25 (21.7)	
<b>Abortion:</b>				
no	158 (68.7)	85 (73.9)	73 (63.5)	p > 0.112
1	47 (20.4)	17 (14.8)	30 (26.1)	
2	16 (7.0)	7 (6.1)	9 (7.8)	
3 ≤	9 (3.9)	6 (5.2)	3 (2.6)	
<b>Early birth:</b>				
No	189 (82.2)	103 (89.5)	86 (74.8)	p < 0.009
1	34 (14.8)	9 (7.8)	25 (21.7)	
2	5 (2.1)	2 (1.8)	3 (2.6)	
3 ≤	2 (0.9)	1 (0.9)	1 (0.9)	
<b>Dead birth:</b>				
No	204 (88.7)	103 (89.6)	101 (87.8)	p > 0.237
1	22 (9.6)	10 (8.6)	12 (10.5)	
2	3 (1.3)	1 (0.9)	2 (1.7)	
3 ≤	1 (0.4)	1 (0.9)	-	

characteristic of groups about blood conflict, smoking, alcohol, fever, and infectious disease underdone during pregnancy, the results were similar between the two groups except smoking (Table 3).

The 92.3% of the women in-group 1 did not have any health problem during pregnancy similar to group 2 (94%). Amniocentesis was done to 3.6% of group 1 while 7% in group 2. Because the age and undeveloped percentage of the both group was same. X ray evaluation was not different between the groups (3.5% in both groups), however, CT evaluation revealed significant difference between groups (control 2.6% and patients 0.9%,  $p = 0.000$ ). It must also be noted that control group had more CT evaluation. As the level of radiation was below critical levels, it could be suggested that it did not affect the frequency of abnormally (Table 4).

## DISCUSSION

By determining the etiological factors causing birth abnormalities, we aimed to determine priorities of

preventive approaches for these abnormalities. The most important factors that could cause these abnormalities were advanced mother age at birth, high rate of consanguine marriage, high rate of smoking. The first step of preventive approach could be acknowledging community about these risk factors. If these preventable factors are eliminated the rate of abnormalities, which are a burden both for the family and the community will be decreased.

There have been amazing advances in embryology, teratology, reproductive biology, genetics, and epidemiology in the past 50 years that have provided scientists and clinicians with a better perspective on the causes of congenital malformations. We still cannot provide the families of children with malformations a definitive diagnosis and cause in every instance.<sup>3</sup>

The suspected external agents have amounted to a handful of infectious, metabolic, endocrinological, environmental, and pharmaceutical culprits,

**TABLE 3:** The background of behavior and infection.

	No. (%) of subjects			statistics
	total	controls	cases	
<b>Blood conflict:</b>				
Yes	28(12.1)	15(13)	13 (11.3)	
No	188(81.7)	91(79.2)	97 (84.3)	
Not knowing	14 (6.2)	9(7.8)	5 (4.4)	p > 0.467
<b>Smoking:</b>				
No	178(77.4)	90(78.3)	88 (76.5)	
Yes	52(22.6)	25(21.7)	27 (23.5)	p < 0.046
<b>Alcohol:</b>				
No	226(98.3)	113(98.3)	113 (98.3)	
1-2 glass/day	4(1.7)	2(1.7)	2 (1.7)	p > 0.101
<b>Fever disease during pregnancy:</b>				
No	212(92.2)	107(93)	105 (91.3)	
Yes	18(7.8)	8(7)	10 (8.7)	p > 0.461

**TABLE 4:** The history of chronic disease, radiologic examination and amniocentesis.

	No. (%) of subjects			statistics
	total	controls	cases	
<b>Illness of pregnant:</b>				
None	214 (93.1)	106 (92.3)	108 (94)	
Diabetes Mellitus	4 (1.7)	2 (1.7)	2 (1.7)	
Hypertansion	4 (1.7)	2 (1.7)	2 (1.7)	
Guatr	5 (2.2)	2 (1.7)	3 (2.6)	p>0.374
Psychiatric Affection	3 (1.3)	3 (2.6)	-	
<b>Radiologic study:</b>				
<b>X-ray:</b>				
Yes	8(3.5)	4 (3.5)	4 (3.5)	p>0.158
No	222 (96.5)	111(96.5)	111 (96.5)	
<b>CT:</b>				
Yes	3 (1.3)	3 (2.6)	1 (0.9)	
No	227 (98.7)	112 (97.4)	114 (99.1)	p<0.000
<b>Amniocentesis reason:</b>				
Not done	218 (94.7)	111 (96.4)	107 (93)	
35 ≤ age	2 (0.9)	1 (0.9)	1 (0.9)	
Undeveloped baby	2 (0.9)	1 (0.9)	1 (0.9)	
Faulty mature	5 (2.2)	1 (0.9)	4 (3.5)	p> 0.562
Genetic disease of parents	3 (1.3)	1 (0.9)	2 (1.7)	

sometimes prematurely incriminated and later absolved. Systematic attempts to sum up the knowledge of what is known and what is left to know about the causation of congenital malformations have all pretty much come to the same 'bottom line'. No further evaluation with any originality has been made for some years now, so it appears we can get to a standstill in this matter.

The purpose of this article is to determine the personal peculiarity, behavioral and environmental differences between the mothers of the groups of normal and defected birth child. This was a retrospective definitive study, which exposed the seriousness of factors determined previously. The systematic consideration of the serious factors can lead to a fresh awareness of risk and

possible strategies toward recognizing and avoiding such risks.

In our study group when we look at the introducer characteristics, we notice that the age of pregnant was important because there was a significant difference on the  $35 \leq$  age. In group 1 19.2% while in group 2 35.6%. The effect of maternal age as a risk factor for Down syndrome is well known. Down syndrome is the most common chromosomal anomaly associated with mental retardation. This is due to the occurrence of free trisomy 21 (92-95%), mosaic trisomy 21 (2-4%) and translocation (3-4%). Advanced maternal age is a well-documented risk factor for maternal meiotic nondisjunction. Besides the other known risk factors, in our study we had an agreement about mother's age is a risk factor for the occurrence of Down syndrome.<sup>9-11</sup>

When we compared the education level, work status, age of marriage and kinship of the husband between the two groups, first three properties were similar but the kinship of the husband was significantly different. Turkey is one of the countries with a high rate of consanguineous unions in the Middle East. The prevalence of consanguinity was found to be 30.6% in Kahramanmaraş. The results of this city revealed differences between consanguineous and non-consanguineous matings, in terms of stillbirth, infant mortality, and birth defects whereas the rate of spontaneous abortion was found to be the same in two kinds of marriages.<sup>12</sup> The total consanguinity was 35.2%, rates being 39.6 and 28.3% for rural and urban areas, respectively in Antalya, a region in the Mediterranean coast of Turkey. Differences were observed between consanguineous and non-consanguineous marriages in sterility, infant death, spontaneous abortion, child death, and congenital malformations, these being significantly higher in consanguineous mating.<sup>13</sup> Turkey has a high rate of consanguineous marriage (21.1%), indicating strong preference for this traditional form of marital union.<sup>14,15</sup> According to the results of our study, consanguineous mating is a significant determinant underlying the abnormal birth rates in Sakarya City in Turkey. A reduction of consanguinity rate is necessary for the health quality of the population.

Number of pregnancies, live children, and premature births were significantly higher in patients' group. Factors such as consanguineous marriage may increase the risk of genetic abnormalities and this may be the cause of higher premature birth rates in this group. There were no significant difference between the groups regarding frequency of abortion and stillbirths.

Smoking is another point to attach the importance by the pregnancies. There is no noteworthy study pointing out the smoking ratio of pregnant women in Turkey. In this study, there was a significant difference between the group 1 (21.7%) and group 2 (23.5%) concerning smoking during pregnancy.<sup>16</sup> Doctors, nurses, midwives and all the surroundings can effectively provide education and support for smoking change during pregnancy if they match the woman's readiness to make changes with the type of advice and support they provide.<sup>17,18</sup> Health education about smoking that is built on co-operation and dialogue was seen by the midwives as a productive way of working. The starting point should be the lay perspective of a woman, which means that her thoughts about smoking cessation are given the space to grow while she talks.

The data regarding the prevalence and patterns of alcohol consumption among 413 pregnant women in the Russian Federation, 347 (85.0%) reported some alcohol consumption during one of the 2 periods, and 193 (51.9%) of these drinking women reported some alcohol use in the most recent month. Reverse of many countries as Russia, researchers did not feel the need for studying the pregnant alcohol use because it is in rare use in Turkey.<sup>19</sup> Both of the groups in this study showed low percentage in alcohol use (1.7%) The evaluation of chronic and acute disease as diabetes, heart disease, hemorrhage, hypertension, goiter, epilepsy and psychiatric disease did not supply us a meaningful datum. The incidence of these previous diseases was low in our study group.

There has been growing concern about radiation exposures in the case of pregnant women who undergo radiological examinations of the lower ab-

domen and pelvis, when the embryo/fetus is near or included in the X-ray field. We did not draw a conclusion that radiological examination is the cause of abnormalities because the samples were not conforming to this. Also for all lower dose examinations of the pelvic area on potentially pregnant patients, special attention is to be given to justifying (or delaying, if appropriate) the examination and, if justified, it is necessary to ensure that the fetal dose is kept to the minimum consistent with the diagnostic purpose.<sup>20,21</sup>

## CONCLUSION

The results were discussed based on the frequency of influential risk factors in Sakarya. We draw a definite conclusion that the pregnancy age and consanguinity of the couples were the major factors that cause faulty birth in this region. The custom of consanguineous unions in the rural population of Turkey is still extremely high, and preventive measures should be done to decrease its frequency and associated complications.

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