

## Moderating effect of maternal characteristics on the relationship between consanguineous marriage and growth quality in Turkish neonates

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### Abstract

The findings regarding the effect of consanguineous marriage on the growth pattern of neonates, which increases the rate of recessive hereditary diseases by causing a decrease in the number of homozygous loci, are controversial. In this study, the effects of consanguineous marriage on the growth pattern of neonates are discussed when the effect of some maternal characteristics is controlled. Two hundred and twenty-five healthy neonates and their mothers born at the Sivas Cumhuriyet University Neonatology Clinic are examined within the scope of the study; 100 of them formed the group of relatives, and 125 of them formed the non-relatives group. The weight, height, head, and chest girth measurements of the babies were taken, and the weight and height of the mothers were measured; the information regarding the age, number of pregnancies, the number of live births, and education levels were recorded. It is observed that first-degree cousin marriages have no detectable effect on the four anthropometric mean vectors of male and female neonates when the effects of maternal characteristics are controlled. In conclusion, it can be said that the strongest maternal effect on the growth level of neonates is the mother's education level; this factor is the strongest moderator variable that controls the effect of consanguineous marriage.

KEYWORDS: consanguinity, first-cousin marriage, neonate, growth, maternal effects

## Introduction

Studies have shown that 10% of marriages worldwide occur between first-degree cousins (Bittles & Black, 2010). Particularly in many countries in Africa and the Middle East and countries such as India and Pakistan, consanguineous marriage is quite common (Mukherjee & Lakshmanudu, 1990; Bittles, 2002; Bener & Al-Ali, 2006; Sharma et al., 2021). Though they are at a negligible level in Western countries, in ethnic communities in North America such as the Amish, the Mennonites, the Hutterites and the Mormons, traditional consanguineous marriages are culturally widespread (Hammond & Jackson, 1958; Jordie, 2001).

In Turkey, where the majority of the population are Muslim, the rate of consanguineous marriages shows a similarity to typical Middle Eastern countries. According to the Turkey Demographic and Health Survey (TDHS, 2018), the rate of consanguineous marriages is 24% nationwide. This rate is 22% in urban areas where the income and prosperity level is relatively higher, while it goes up to 29% in rural areas. When looked at from a regional perspective, the significant difference in the rates of consanguineous marriages is striking. While consanguineous marriage is preferred by 43% in the cities located in the Southeast Anatolia region, this rate falls to 10% in the West Marmara region (TDHS, 2018).

It is observed that the factors that encourage consanguineous marriages are primarily religious, cultural, traditional and/or economic reasons. There is a widespread belief that marriages between couples with consanguinity strengthen family ties, protect family property and increase marriage harmony (Abbas & Yunis, 2014). In contrast, it is observed that consanguineous marriages are usually preferred by couples who have low social status, marry at a young age, have lower levels of education, and live in rural areas (Kaplan et al., 2016).

For a long time, studies conducted on consanguineous marriages have focused on the clinical effects of inbreeding. It is known that inbreeding decreases heterozygosity by revealing harmful recessive alleles and that it causes low birth weight and preterm delivery as well as various genetic diseases (Mumtaz et al., 2007; Poorolajal et al., 2017). However, there is not a total consensus in the literature regarding the effect of consanguineous marriage on prenatal growth quality. Many studies show that inbreeding does not lead to growth retardation in neonates (Rao & Inbaraj, 1980; Asha & John, 1982; Başaran et al., 1994).

In previous studies conducted on neonates at Sivas, it was revealed that inbreeding did not cause an increase in fluctuating asymmetry levels (Özener & Graham, 2014), but that

it led to masculinisation in terms of the second to fourth digit ratios (2D:4D) (Ertuğrul & Özener, 2020). In this study, when the effects of some variables (mother's education level, height, weight, body mass index, number of pregnancies, and number of live births) are controlled, the effect of consanguineous marriage on the growth patterns of neonates will be examined.

## **Materials and methods**

### **Sample**

The study was conducted at the Neonatology Clinic of Sivas Cumhuriyet University Medical Faculty Hospital. This hospital is the only university hospital in Sivas, and the majority of the families visiting the hospital belong to medium/low socioeconomic segments of society. Mostly lower/medium socioeconomic families apply to this clinic, where five to six deliveries occur per day. The study group consisted of neonates born in term between the 37<sup>th</sup> and 41<sup>st</sup> weeks of pregnancy. The mean gestation age did not differ between relative and non-relative groups ( $F_{1,224} = 1.41, P = 0.24$ ).

Within the scope of the study, 225 healthy neonates and their mothers were examined; 100 of them constituted the relative group, while 125 were not relatives. The most preferred consanguineous marriage type in Turkey is first-degree cousin [ $f$  (coefficient of inbreeding) = 1/16] marriages (see Kaplan et al., 2016). The relative group was chosen among the mothers who had married a first-degree cousin (marriage uncle and aunt children), and the individuals in the non-relative group were chosen among the mothers who had no genetic bonds [ $f = 0$ ].

With the survey conducted before the measurement of the neonates and mothers, the mothers' date of birth, the number of pregnancies, the number of live births, and education levels were determined

### **Physical measurements**

Next, the physical measurements of the mothers were made. Mothers stood on the anthropometer boards (Seca 213) without shoes, with their heels in a joint and vertical position and the head on the Frankfurt plane; measurements were made by touching the movable arm of the anthropometer on the vertex (i.e., the highest point of the head). Weight measurement was made without shoes and with minimum clothes on a Tania brand scale sensitive to 100 grams (Lohman et al., 1988)

The supine lengths of the neonates were measured in a lying position on their back and without diapers were a Seca 207 model infantometer compatible with Holtain brand stadiometers (Cogill, 2003). Measurements were made while the head of the neonate was on the Frankfurt plane, the hip and shoulder centres were in a vertical position, and the knees were gently pressed, the fixed arm was touched on the vertex, and the movable arm was touched on the heels in 90 degrees vertical position. In order to determine the weight, a 10 g sensitive Seca 354 digital infant scale was used while the neonates were naked.

Head circumference was measured with the help of an inflexible and 0.6 cm wide tape at 0.5 mm sensitivity. The tape was wrapped around the head just above the eyebrow arch and passing from the most protruding section of the head, and the widest measurement of the head was thus obtained. As for the measurement of the chest, the tape was wrapped around the chest on the nipple line, and measurement was made. Prior to the measurement of the infants, parents were asked to voluntarily complete informed consent forms approved by the Ethics Committee of Cumhuriyet University.

### **Statistical analyses**

In order to test whether the neonates of the parents who had consanguineous marriages were smaller in terms of physical development, Multivariate Analysis of Covariance (MANCOVA) was employed, and in the analyses, weight, height, head and chest circumference were used as dependent variables, while the marriage type (consanguineous and non-consanguineous) was used as the independent variable (fixed factor). The control variables such as mother's age, height, body mass index, number of pregnancies, number of live births, and education level, which are accepted as maternal effects, were considered co-variables.

In the Univariate Analysis of Covariance (ANCOVA), in contrast, the neonates' weight, height, and head and chest circumferences were taken as dependent variables, while marriage type (consanguineous and non-consanguineous) was accepted as an independent variable, and mothers' education level (years) as a control variable (co-variable). All analyses were done separately for each sex.

### **Results**

Descriptive statistics of the two groups are presented in Tables 1 and 2. The neonates included in the consanguineous group have lower values for both sexes in terms of

weight. In addition, it was determined that the female neonates in the consanguineous group had lower values in terms of head circumference. The differences observed in terms of the mother's education level, number of pregnancies, and number of live births were significant in the consanguineous and non-consanguineous groups. It is seen that the mothers of the male neonates in the consanguineous group had 3.48 years less education, while the mothers of the female neonates in the consanguineous group had 2.81 years less education.

*Table 1: Descriptive statistics of general characteristics of mothers and their male neonates*

	<b>Consanguineous</b>		<b>Nonconsanguineous</b>		<b>F</b>	<b>P</b>
	<b>Mean</b>	<b>SD</b>	<b>Mean</b>	<b>SD</b>		
<b>Mother</b>						
Age (year)	27.21	4.44	28.39	4.19	1.74	0.19
Height (cm)	158.90	6.91	161.10	7.50	2.13	0.15
BMI (kg/m <sup>2</sup> )	29.45	4.34	28.62	4.27	0.86	0.36
Number of pregnancy	3.05	1.74	2.76	1.52	0.74	0.39
Number of live births	2.84	1.41	2.16	0.94	7.53	<b>&lt;0.01</b>
Education level (year)	5.64	2.05	9.12	3.78	29.62	<b>&lt;0.001</b>
<b>Neonate</b>						
Weight (kg)	3.19	0.42	3.46	0.64	5.83	0.02
Height (cm)	50.18	1.70	50.78	1.85	2.56	0.11
Head circumference (cm)	35.20	0.96	35.35	0.98	0.51	0.48
Chest circumference (cm)	33.51	0.95	33.59	1.22	0.11	0.75

*Table 2: Descriptive statistics of general characteristics of mothers and their female neonates*

	<b>Consanguineous</b>		<b>Nonconsanguineous</b>		<b>F</b>	<b>P</b>
	<b>Mean</b>	<b>SD</b>	<b>Mean</b>	<b>SD</b>		
<b>Mother</b>						
Age (year)	27.45	4.28	27.42	4.27	0.01	0.96
Height (cm)	158.98	5.91	161.21	7.11	3.28	0.07
BMI (kg/m <sup>2</sup> )	29.06	3.99	28.70	4.97	0.18	0.67
Number of pregnancy	3.21	1.51	2.52	1.22	6.97	<b>&lt;0.01</b>
Number of live births	2.67	1.14	2.29	1.22	2.90	0.09
Education level (year)	5.79	2.56	8.60	2.04	19.83	<b>&lt;0.001</b>
<b>Neonate</b>						
Weight (kg)	3.01	0.42	3.28	0.52	4.92	<b>&lt;0.05</b>
Height (cm)	49.99	1.31	50.36	1.66	1.69	0.20
Head circumference (cm)	34.79	0.99	35.13	0.79	4.30	<b>&lt;0.05</b>
Chest circumference (cm)	33.25	0.84	33.48	0.95	1.94	0.17

According to the Multivariate Analysis of Covariance performed in order to test the null hypothesis in which the mean vectors of the neonates whose parents were in consan-

guineous and non-consanguineous groups were sampled from the same group, it is seen that after the elimination of the effects of maternal characteristics, first-degree cousin marriages do not have a significant effect on the four anthropometric mean vectors of male and female neonates (Table 3). The Multivariate Analysis of Covariance showed that for male neonates, the mother's height and education level had a primary effect on the weight, height, head circumference, and chest circumference development levels of the neonates, while for female neonates, the mother's education level had an important effect in this respect.

Table 3: Multivariate analyses of covariance for male and female neonates

Sex	Variable*	Wilk's $\lambda$	F	P
<b>Male</b>	<b>Marriage type</b>	0.93	1.56	0.19
	<b>Age</b>	0.93	1.51	0.21
	<b>Height</b>	0.86	3.52	<b>&lt;0.05</b>
	<b>BKI</b>	0.91	2.01	0.10
	<b>Number of pregnancy</b>	0.95	1.05	0.39
	<b>Number of live births</b>	0.97	0.61	0.66
	<b>Education level</b>	0.89	2.46	<b>&lt;0.05</b>
<b>Female</b>	<b>Marriage type</b>	0.98	0.52	0.72
	<b>Age</b>	0.96	1.24	0.30
	<b>Height</b>	0.98	0.64	0.64
	<b>BKI</b>	0.93	2.19	0.75
	<b>Number of pregnancy</b>	0.97	0.83	0.51
	<b>Number of live births</b>	0.94	1.85	0.12
	<b>Education level</b>	0.85	4.76	<b>&lt;0.01</b>

\*Dependent variables: weight, height, head circumference, chest circumference of the neonates; independent variable (fixed factor): marriage type of the mother; co-variables: mother's age, height, BMI, number of pregnancy, number of live births, education level

Table 4: Univariate analyses of covariance for male and female neonates

Sex	Variable*	Marriage type				Education level			
		DF	MS	F	P	DF	MS	F	P
<b>Male</b>	Weight	1	3.63	1.26	0.27	1	12.28	4.18	<b>&lt;0.05</b>
	Height	1	0.01	0.04	0.84	1	0.19	11.24	<b>&lt;0.01</b>
	Head circumference	1	0.01	1.36	0.25	1	1.15	13.58	<b>&lt;0.001</b>
	Chest circumference	1	0.02	1.87	0.18	1	1.23	11.28	0.001
<b>Female</b>	Weight	1	0.02	0.99	0.32	1	2.20	9.03	<b>&lt;0.01</b>
	Height	1	0.02	0.79	0.40	1	0.01	0.79	0.38
	Head circumference	1	0.03	2.48	0.12	1	0.07	0.86	0.36
	Chest circumference	1	0.16	1.83	0.18	1	0.01	0.03	0.86

\*Dependent variable: marriage type of the mother; co-variable: mother's education level

According to the Univariate Analysis of Covariance results, while all dependent variables differed according to the mother's education year in male neonates, in female neonates, only the value of weight was affected by the mother's education level (Table

4). It was observed that mothers with more years of education tended to give birth to heavier and taller male neonates with bigger head and chest circumferences and heavier female neonates.

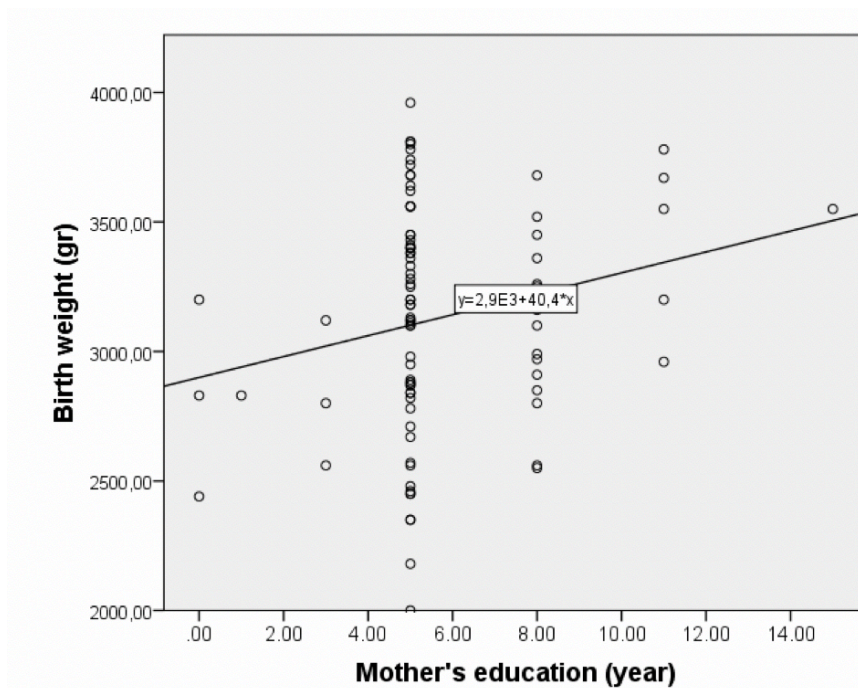


Figure 1: The relationship between the weight of the neonates (male & female) and the mother's education level in the consanguineous group

The analysis also revealed (Figure 1) that as the mother's education level increased, the restrictive effect of consanguineous marriage on growth decreased ( $r_{\text{Pearson}} = 0.22$ ,  $P = 0.036$ ).

## Discussion

In the study, it was determined that when maternal effects as independent variables were controlled, inbreeding did not significantly affect the growth quality of neonates, in contrast to expectations. Although many epidemiological studies have shown that the babies of children of parents who were relatives are retarded in terms of growth (Mumtaz et al., 2007; Poorolajal et al., 2017), a considerable number of studies do not confirm these findings (See Rao & Inbaraj, 1980; Asha & John, 1982; Bařaran et al., 1994). In a study conducted by Bařaran et al. in Turkey, certain anthropometrical characteristics of 2880 neonates were examined, and it was concluded that the differences were not significant, although some measurements were low to a certain degree in the babies of first-

degree cousin couples. In the aforementioned study, it is seen that the moderating variables were not considered, and the researchers concluded that kinship alone did not have a significant effect on multi-factor characteristics (Başaran et al., 1994).

Most of the information in the literature on the relationship between the growth quality of neonates and consanguineous marriage is based on the studies conducted in India and countries in the Middle East. In one of the early period studies conducted on this issue, Rao and Inbaraj (1980) investigated 14,243 neonates born in the Tamil Nadu region of India. The babies of families living in rural areas were examined, and no effect of consanguineous marriage on the weight of the neonates was revealed. The findings of the study that Asha and John (1982) carried out in the same region on first-degree cousin marriages are similar. In contrast, when first-degree cousin marriages are considered, in the studies conducted in Pakistan (Honeyman et al., 1987), Lebanon (Khlaf & Khudr, 1984), Saudi Arabia (al-Abdulkareem & Balla, 1998; Belal et al., 2018), and Morocco (Fried & Davies, 1974), it was determined that consanguineous marriages had no negative effects on the growth pattern of the neonates. The common point of these studies is that they considered only birth weight but did not evaluate environmental factors such as maternal characteristics, which are known to be effective on prenatal development. It is clear that studies in which the social status of the sample is considered are more reliable. The most comprehensive study in which various environmental factors were controlled was conducted by Mumtaz et al. in Lebanon (2007). Conducted on 10,289 neonates with 28-42 weeks gestational age, the study considered many variables, such as the mother's age, anthropometric properties, education level, number of pregnancies and live birth, and smoking habit. The findings obtained from multiple regression analysis revealed that first-degree cousins tended to give birth to babies with lower weight when the environmental effects were taken under control. The most striking finding in that study is that a decrease in the mother's education level and an increase in smoking habit made this tendency more pronounced by creating a moderating effect (Mumtaz et al., 2007).

In the present study carried out in Sivas, it was found that mothers who had kinship with their husbands were shorter ( $F_{1,224} = 5.52, P < 0.05$ ), had more number of pregnancies ( $F_{1,224} = 6.26, P < 0.05$ ) and live births ( $F_{1,224} = 9.73, P < 0.01$ ), and their educational periods were three years shorter ( $F_{1,224} = 47.26, P < 0.001$ ). With these characteristics, it can be claimed that the mothers in the consanguineous group are exposed to intense more stress compared to the mothers in the other group.



A variety of studies show that the size of the effect of inbreeding depends on the level of environmental stress experienced by the organisms during their developmental stage. This situation means that a statistical interaction exists between genetic and environmental stresses. It is seen that under optimal conditions, the fitness capacity of inbred, hybrid individuals is as good as the individuals who are not genetically relatives (Lens et al., 2000).

Nevertheless, the information on this issue is based on studies on other species rather than on humans. Meagher et al. (2000) examined inbred hybrid *Mus musculus* in their natural habitat and in laboratory conditions. It was observed in the study that the fitness capacities of male rats which lived under stress load in natural conditions decreased by 81%, while those who lived in less stressed laboratory conditions had a lower decrease in adaptation capacities by 11%. If the relationship between inbreeding and growth capacity is affected by environmental stresses, the size of the relationship between physical development and consanguineous marriage may depend on how much stress has been experienced during prenatal development (See Miller, 1994). While the difference between the neonates born in Sivas becomes clearer in families with low socioeconomic status, especially as the mother's level of education increases, the pressure of inbreeding decreases (Figure 1). In contrast, the effect of maternal education level on growth becomes more evident (also see Khanra et al., 2021). This finding supports the view that there is a statistical interaction between genotypic pressures and environmental stresses.

However, it is also known that consanguineous marriage increases the prevalence of preterm delivery (Kramer et al., 2001). Our study group was composed of neonates born at term; therefore, data on preterm neonates are not within the scope of this study. In a study conducted in Jordan, it was determined that preterm delivery was the primary cause of the differences in birth weight between the neonates in the relative group and the non-relative group (Obeidat et al., 2010). Similar results were obtained in the study carried out by Mumtaz et al. (2010). At the same time, there are many studies in which it was found that height development in babies of relative parents was retarded. The findings of this study may imply that the pressure of inbreeding shows its effect in the post-natal development process. To illustrate, in a study conducted in Ankara, it was determined that young males whose parents are first-degree cousins were 3.5 cm shorter than their peers in the group with no genetic kinship (Özener, 2010). Similar results were observed in the studies conducted in Pakistan (Chauhan et al., 2020) and India (Krishan, 1984; Fareed & Afzal, 2014).

In conclusion, our study conducted on 225 healthy neonates whose parents were first-degree cousins suggests that—when maternal factors are taken into account—the effect of consanguineous marriages on the growth quality of neonates decreases. It can be stated that the most powerful effect on especially growth level is the mother’s education level, and that mother’s education level is the strongest moderating variable that controls the effect of consanguineous marriages.

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### **Povzetek**

Ugotovitve o vplivu sorodstvene zakonske zveze na vzorec rasti novorojenčkov, ki povečuje stopnjo recesivnih dednih bolezni z zmanjšanjem števila homozigotnih lokusov, niso enotne. v pričujoči študiji proučujemo učinke sorodstvene poroke na vzorec rasti novorojenčkov, če nadzorujemo učinek nekaterih materinih značilnosti. V okviru študije smo proučili dvesto petindvajset zdravih novorojenčkov in njihovih mater, rojenih na Univerzitetni neonatološki kliniki Sivas Cumhuriyet; 100 jih je sestavljalo skupino sorodnikov, 125 pa skupino nesorodnikov. Izmerili smo težo, višino, glavo in obseg prsnega koša dojenčkov ter težo in višino mater; evidentirani so bili podatki o starosti, številu nosečnosti, številu živorojenih otrok in stopnji izobrazbe. Pokazalo se je, da poroke bratrancev nimajo zaznavnega učinka na štiri antropometrične povprečne vektorje novorojenčkov moškega in ženskega spola, če so učinki materinih značilnosti nadzorovani. Sklepamo lahko, da je najmočnejši materinski učinek na stopnjo rasti novorojenčkov izobrazba matere; ta dejavnik je najmočnejša spremenljivka moderatorja, ki nadzoruje učinek zakonske zveze v sorodstvu.

KLJUČNE BESEDE: sorodstvo, poroka bratrancev, novorojenček, rast, materinski učinki

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