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Analysis of perinatal outcomes of pregnancies from consanguineous marriages in a tertiary hospital in Bursa, Turkey

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ABSTRACT

Aim: In this article, we aimed to contribute to the outcomes of the consanguineous marriage literature by analyzing fetal results in this population.

Material and Method: We included 185 patients in this retrospective research. Demographic, clinical, ultrasonographic and delivery data were received from electronic patient records. Also, we recorded the postnatal results, and findings of the infants. By combining all the data, we reported a descriptive analysis of the results of our consanguineous marriage cases with perinatology follow-up.

Results: We had 231 pregnant women in the study, and their mean age was 28.9 years. 117 (50.6%) of the pregnant women had first-degree, and 114 (50.4%) had second-degree consanguineous marriages. Fetal findings were evaluated as usual in 157 (68%) of the pregnant in the ultrasonographic scans performed between prenatal 20-24 weeks of gestation. When we look at the first postnatal examinations of the babies, no abnormal findings were in 134 babies (58.8%). Twenty-two infants (9.6%) were followed up in the neonatal intensive care unit with the diagnosis of transient tachypnea of the newborn, and phototherapy was required in 14 infants (6.1%) due to hyperbilirubinemia. The number of cases requiring surgical intervention after delivery or with significant life-threatening anomalies included 56 findings in 32 infants. There were spina bifida cases in 8 infants and hydrocephalus in 9 infants.

Conclusion: There was an increased level of congenital anomalies associated with consanguineous marriages. Health care centers should educate individuals regarding the negative role of cousin marriages leading to abnormalities in children.

Keywords: Consanguinity, perinatology, congenital abnormalities, down syndrome

INTRODUCTION

Consanguineous marriage (CM) has been traditionally practiced by many societies worldwide since ancient times (1). Consanguinity is a mixture of two Latin words: "con" means similar, and "sanguineus" means blood. It indicates an association between people who have an identical forefather or belong to the same blood. The kindred ship is often referred to as an association shared by two biologically related people (2). In the medical literature, it is generally defined as the union of a second cousin or closer couple (3). The most common form of CM is between first cousins of both mothers and fathers. Consanguinity is a cultural practice in many countries, and around 10% of the population worldwide are married to biological or blood relatives (1).

The prevalence of CM, the union between two people who are related as second cousins or closer, varies globally, with rates as low as 5% in the USA, Western Europe, and Australia and up to 70% in regions such as the Middle East (4).

Marriage between related individuals has resulted in several adverse outcomes among children. Several studies have reported an increased risk of death among the children of consanguineous couples. The most commonly studied and well-known association with CM is congenital anomalies. Offspring of related individuals are more likely to have rare autosomal recessive diseases that are uncommon in children of non-consanguineous couples. Absolute risk changes by population, and the outcome was 1.7–2.8% higher for the children of first cousins than those from non-related couples (4–6).

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Consanguineous marriage is one of the predisposing factors for multifactorial complications, like obesity, cardiovascular disorders, diabetes, and malignancies, which influence reproductive outcomes (7,8). These marriages are associated with higher rates of congenital disabilities, as are several single-gene and multifactorial diseases (9,10).

CM may also result in spontaneous abortion (SAB), a common outcome occurring in 15–20% of all clinically recognized pregnancies. Chromosomal abnormalities are implicated in approximately 50% of early losses (4,11). It is recommended that consanguineous couples be offered genetic counseling to discuss the increased risk of recessive disease in their offspring and the increased risk of stillbirth or perinatal death (5).

In this article, we reported the obstetric analysis of consanguineous marriage cases who applied to our obstetrics outpatient clinics and had perinatology follow-ups with any fetal reason. We aim to contribute to the results of the consanguineous marriage literature by analyzing fetal outcomes in this population.

MATERIAL AND METHOD

The study was carried out with the permission of Bursa Yüksek İhtisas Training and Research Hospital Clinical Researches Ethics Committee (Date: 24.08.2022, Decision No: 2011-KAEK-25 2022/08-15). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

In this retrospective study, we included 231 pregnancies who applied to our tertiary care hospital between 2019-2022 and were followed up by perinatology due to consanguineous marriage. In our department, in our daily practice, first-trimester drug use, bad obstetric history, excessive first-trimester nuchal translucency, high risk detected in double triple or quadruple test, a major or soft anomaly sign detected on ultrasonography, placental invasion anomaly, consanguineous marriage, or We refer pregnant women with a history of babies with abnormalities in their previous pregnancy to perinatology control. In this study, we evaluated only the patients included in perinatology follow-up due to consanguineous marriage. Thus, we aimed to make a homogeneous contribution to patient standardization.

Demographic, clinical, ultrasonographic, prenatal genetic diagnosis, and delivery data were obtained from electronic patient records. We recorded the postnatal examination findings, gestational week, fetal birth weight, intensive care observations, and diagnoses of the infants. Pathological conditions detected as a result of the examination were divided into groups according to organ systems. All couples were told to receive genetic counseling and to apply to the genetic diseases' diagnosis-screening department.

We also noted the birth findings of the mothers, the birth complications, if any, and the mode of delivery.

Statistical Analysis

For proper statistical analyses, Windows-based SPSS 24.0 statistical analysis program was used (SPSS Inc., USA). To determine whether they were normally distributed or not, variables were examined via visual (histograms, probability plots) and analytical methods (Shapiro-Wilk's test). Variables were descriptively specified as mean±standard deviation (X±SD), mean difference between groups, 95% confidence interval (95%CI), median (minimum-maximum (min-max)), U value, frequency (n) and percentage (%).

RESULTS

In this study, we analyzed the follow-up of consanguineous pregnancies who applied to the perinatology outpatient clinic of our tertiary hospital and whose obstetric and neonatal outcomes are also available. We had 231 pregnant women in the study, and their mean age was 28.9 years. 117 (50.6%) of the pregnant women had first-degree, and 114 (50.4%) had second-degree consanguineous marriages. All pregnancies were singleton pregnancies. While the ethnicity of 191 (82.7%) patients was Turkish, the race of 40 patients (17.3%) was Syrian. One hundred forty-five of the deliveries were by cesarean section (63.6%), and 83 were by vaginal delivery (36.4%). Among the indications for cesarean section, the most common reason was previous uterine surgery (n=70, 48%). Other causes were acute fetal distress (n=43, 29%), cephalopelvic disproportion (n= 18, 1.2%), surmaturation (n=9, 0.6%), other (n=5, 0.3%), respectively. Three pregnancies were terminated after amniocentesis with the diagnosis of Down syndrome (The ages of these pregnant women were 23, 25 and 35.). The mean weight of babies born in the 2nd or 3rd trimester was 2920±565.4 grams. The third trimester birth weight was 2984.9±508.2 grams, while the second trimester was 604±104 grams. The median value of the weeks of birth was 38 weeks (24-40). While 149 (65.4%) babies were given to their mothers after birth, 77 (33.3%) were followed in the neonatal intensive care unit. Only 34 of the pregnant women who were offered genetic counseling were interested in this issue, and this rate remained at 14 percent among all pregnant women. The relevant analysis is summarized in **Table 1**.

Table 1. Descriptive analyses of values regarding the mothers and the babies

Characteristics of mothers and babies	Pregnant women (n= 231) X±SD/Median (min-max)
Age (year)	28.9 ± 6.9
Parity	2 (0-6)
Week of birth	38.3 (24-40)
Birth weight (gr)	2920±565.4
Postpartum with mother, breastfeeding (n;%)	149; 65.4%
Neonatal intensive care (n;%)	77; 33.3%
Intrauterine ex fetus (n;%)	2; 0.8%
Postpartum death in first 24 hour (n;%)	6; 2.6%
Termination (n;%)	3; 1.3%
Degree of kinship (n; %)	
First degree	117 (50.6%)
Second degree	114 (%50.4)
Race	
Turkish	191 (82.7%)
Syrian	40 (17.3%)
Method of delivery	
Ceserean	145 (62.8%)
Vaginal delivery	83 (35.9%)
Termination	3 (1.3%)

gr: gram, n: frequency, %: percentage, X: mean, SD: standard deviation, min: minimum, max: maximum. Descriptive analyses were presented using (X±SD), median (min-max) and (n;%) for normally distributed, non-normally distributed and categorical variables, respectively.

Fetal findings were evaluated as usual in 157 (68%) of the pregnant in the ultrasonographic scans performed between prenatal 20-24 weeks of gestation. Facial defects were observed in 8 (3.4%) of the other fetuses (2 retrognathia, 4 cleft palate-lip, 2 cystic hygroma). There were extremity anomalies in 11 fetuses (4 short limbs, 3 femur bowing) and genitourinary abnormalities in 6 fetuses (4 pelviectasis, 2 polycystic kidneys). In comparison, there were gastrointestinal system findings in 16 (6.9%) fetuses (5 hyperechoic bowels, 4 intestinal atresias, 4 diaphragmatic herniae);and we detected cardiac results (hyperechoic heart in 8 fetuses, vsd in 3 fetuses) in 15 fetuses. The most common finding we noticed in the pregnant women we screened belonged to the central nervous system and these findings were present in 19 fetuses (8.2%). Anomaly involving more than one system was present in ten babies. The entire analysis is summarized in **Table 2.**

While the diagnosis of pregnancy in labor (n=93, 40.8%) constituted the majority of the delivery indications, the number of cases with a history of cesarean section reaching 39 weeks was 51 (22.4%). While delivery was decided due to intrauterine growth retardation in 19 fetuses, 20 pregnant women were subjected to labor induction due to surmaturation (>41 weeks gestational age). The median Apgar values at the 1st minute were 7 (4-9). When we look at the first postnatal examinations of the babies, no abnormal findings were in 134 babies (58.8%). While 22 infants (9.6%) were followed up in the neonatal intensive care unit with the diagnosis of transient tachypnea of the newborn, phototherapy was required in 14 infants (6.1%) due to hyperbilirubinemia. The number of cases requiring surgical intervention after delivery or with significant life-threatening anomalies included 56 findings in 32 infants. More than one anomaly was present in 10 infants. There were spina bifida cases in 8 infants, hydrocephalus in 9 infants, 2 omphaloceles, a cardiac anomaly in 6 infants, intestinal atresia in 4 infants, and 3 diaphragmatic hernia cases. Four babies were born with cleft palate-lip finding. Down syndrome morphology was detected in two babies and both of them were born as intrauterine ex fetuses. One infant had signs of metabolic disease, and one infant had anal atresia. The complete analysis of birth outcomes is available in **Table 3**.

Table 2. Descriptive analysis table of second trimester fetal ultrasonographic screening findings

Findings	Pregnant women (n= 231)
Usual (n; %)	157; 68%
Fascial defects (n; %) Retrognathia (n=2) Cleft palate-lip (n=4) Cystic hygroma (n=2)	8; 3.4%
Extremity anomalies (n; %) Short limbs, achondroplasia (n=4) Bowing of femur (n=3) Claw hand (n=1) Polydactyly (n=1) Rocker bottom feet (n=1) Pes equinovarus (n=1)	11; 4.6%
Genitourinary anomalies (n; %) Pelviectasis (n=4) Polycystic kidney (n=2)	6; 2.6%
Gastrointestinal system findings (n; %) Hyperechoic bowels (n=5) Intestinal atresia (n=4) Diaphragmatic hernia (n=3) Omphalocele (n=2) Anal atresia (n=1) Small gallbladder (n=1)	16; 6.9%
Cardiac findings (n; %) Hyperechoic focus (n=8) Ventricular septal defect (n=3) Cardiomegaly (n=2) Hypoplastic heart (n=1) Hydrothorax (n=1)	15; 6.4%
Nervous system abnormalities (n; %) Hydrocephalus (n=9) Spina bifida (n=8) Cerebellar hypoplasia (n=2) Vermian hypoplasia (n=1) Mega cisterna magna (n=2)	19; 8.1%
Others Kyphoscoliosis (n=2) Hydrops fetalis (n=4)	6; 2.6%
Obstetric findings (n; %) Polyhydramnios (n=6) Oligohydramnios (n=4) Intrauterine growth retardation (n=2) Placenta previa (n=2) Placenta percreata (n=1)	15; 6.4%

n: frequency, %: percentage. Descriptive analyses were presented using (n;%) for categorical variables. There is more than one finding in the same case, and n and percent values were determined according to the total number of volunteers

Table 3. Analysis table according to the findings of the babies in the first 24 hours after birth

Findings	(n= 228) Median (min-max)
Healthy baby (n; %)	134; 58.7%
Transient tachypnea of the newborn (TTN) (n; %)	22; 9.6%
Hyperbilirubinemia (n; %)	14; 6.1%
Sacral dimple (n; %)	16; 7%
Gastrointestinal system findings (n; %) Intestinal atresia (n=4), Diaphragmatic hernia (n=3) Omphalocele (n=2) Anal atresia (n=1)	10; 4.3%
Cardiac findings (n; %) Ventricular septal defect (n=4) Cardiomegaly (n=2) Hypoplastic heart (n=1) Hydrothorax (n=1)	8; 3.5%
Central nervous system abnormalities (n; %) Hydrocephalus (n=9) Spina bifida (n=8) Cerebellar hypoplasia (n=1) Hypotony (n=1)	19; 8.3%
Fascial defects (n; %) Cleft palate-lip (n=4)	4; 1.7%
Extremity anomalies (n; %) Short limbs, achondroplasia (n=4), Bowing of femur (n=3) Polydactyly (n=1) Pes equinovarus (n=1)	9; 4%
Genitourinary anomalies (n; %) Pelviectasis (n=1) Polycystic kidney (n=1)	2; 0.9%
Others Kyphoscoliosis (n=2) Hydrops fetalis (n=2)	4; 1.7
APGAR 1st minute score	7 (4-9)

n: frequency, %: percentage. Descriptive analyses were presented using median (min-max) and (n;%) for non-normally distributed and categorical variables, respectively. There is more than one finding in the same case, and n and percent values were determined according to the total number of volunteers.

DISCUSSION

In this article, we published our research results on the effects of inbreeding on birth outcomes, congenital malformations, and fetal growth/development/health. As genetic and environmental factors can determine such effects, there are dissimilarities among the available reports in the literature.

The concept of kinship is generally defined in clinical usage as a union between two people who are second cousins or more closely related. The most common form of consanguineous marriage worldwide is between first cousins (12,13). The estimation of consanguinity shows that about 10% of the world's population is married to a biological relative (14). However, this estimate is unclear due to the lack of information on consanguineous marriage in many South and Southeast Asian countries and Africa. It is now accepted that variables such as socioeconomic status, maternal age, maternal education, birth order, and birth intervals should be adequately controlled in evaluating the effects of inbreeding on health (6).

Consanguineous marriage is essential due to infant death, miscarriages, and fetal death. Cousin marriage is a significant cause of genetic disorders and congenital disabilities transmitted from parents to children (15). Infant deaths and fetal deaths are some of the consequences of consanguineous marriages (16,17). Cousin marriage can cause congenital heart defects (18). Congenital cardiovascular malformations are common in these associations and affect 2.4 to 8.0 in 1000 infants (19). In our study, prenatal cardiac findings were found in 15 fetuses. In contrast, cardiac pathology was present in 6 (2%) babies after birth (ventricular septal defect in 4 babies, hypoplastic right heart in 1 baby, and cardiomegaly in 2 baby). Six babies who were taken to the neonatal intensive care unit after birth died. Two of these babies had severe hydrocephalus and extremity abnormalities. One baby had a hypoplastic heart, while the other three died with prematurity signs.

The present study showed that 12% of mothers had major congenital abnormalities which required surgical intervention after delivery or had a life-threatening from consanguineous marriages. Mosayebi et al. (20) and Naveed et al. (2) determined this rate to be around 14-15% in their studies. We detected hydrocephalus in 9 infants and spina bifida in 8 infants. Anomaly involving more than one system was present in 10 babies. When we look at the ultrasonographic examination performed in the prenatal period, we found that the pelviectasis findings of 3 babies regressed (75%) after birth, and there was ventricular septal defect in 1 baby who could not be diagnosed prenatally. Naveed et al. detected brain anomalies in 26% of the babies in their study. In their study, Tomatır et al. (21) detected brain anomalies in 12 (31%) cases. In our cases, postnatal brain anomaly constituted 25% of abnormal cases.

One of the interesting parts of our study was the indifference of consanguineous couples to prenatal genetic counseling. Consanguineous couples be offered genetic counseling to discuss the increased risk of recessive disease in their offspring and the increased risk of stillbirth or perinatal death. The fact that only 34 (14%) of 231 couples received genetic counseling during the prenatal period and that other cases did not require it supports the need to increase social awareness of this issue.

There were also some limitations of our study. Some couples who applied with consanguineous marriage did not apply to our department during the follow-up and were excluded from the study, thus reducing the total number of cases. In addition, consanguineous couples were not compared with the average population and there was no control study regarding obstetric outcomes. This study is only descriptive, and we aimed

to contribute to the literature by analyzing the prenatal and postnatal findings and current consanguineous pregnancy outcomes, which we followed up on in our department.

CONCLUSION

There was an increased level of congenital anomalies associated with consanguineous marriages. A wide range of genetic disorders was seen in families having cousin marriages. There should be increased awareness among families regarding the negative impact of cousin marriage. Health care centers should educate individuals regarding the negative role of cousin marriages leading to abnormalities in children.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Bursa Yüksek İhtisas Training and Research Hospital Clinical Researches Ethics Committee (Date: 24.08.2022, Decision No: 2011-KAEK-25 2022/08-15).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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