Epidemiology of congenital anomalies in different ethnicities

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Summary

Purpose of investigation: To study the prevalence and the epidemiologic characteristics of major congenital anomalies (MCAs) in two different populations in Thrace-Greece.

Methods: The ethnic origin of all mothers who delivered in our department and the types of MCAs were determined. We compared the frequencies of MCAs between Christians and Muslims. The chi-square test, t-test, binary and multinomial logistic regression analysis were performed.

Results: The prevalence of MCAs was significantly higher in Muslims as compared to Christians (51/4,028 (12.78%) vs 49/5,994 (8.17%), p = 0.035). However, the frequencies of each type of MCA in the total number of deliveries between the two groups did not differ significantly. The central nervous system malformations were most frequently associated with perinatal mortality.

Conclusion: This is the first study in Greece showing that there is probably a higher prevalence of MCAs in Muslims as compared to Christians, although it can not be elucidated whether this increased risk is related to specific differences between them.

Key words: Major congenital malformations; Epidemiology; Christians; Muslims; Greece.

Introduction

A malformation is a primary error of normal development or morphogenesis of an organ or tissue. All malformations are thus congenital or present at birth, although they may not be diagnosed until later, especially if microscopic or internal organs are involved. In the international literature about 3% of newborns have a single major malformation and 0.7% of newborns have multiple major malformations [1]. In Greece epidemiologic data about the frequencies of major congenital malformations are scanty, although some papers refer to specific types [2, 3] and one publication reports that the prevalence at birth of congenital malformations in Athens, Greece during the period 1955-1965 was 20.62 per 1,000 newborns (live and stillborn infants) [4]. Considering reports in the international literature suggesting ethnic differences in the incidence of malformations, it would be very interesting to investigate for the first time the respective situation in our area.

Thus the aim of the present retrospective study was to examine the differences in the frequencies of major congenital malformations between the two major ethnic groups in the area of Thrace in Greece.

Materials and Methods

The ethnic origin of all mothers who delivered in the Department of Obstetrics and Gynecology of the Democritus University of Thrace was obtained from the labor ward delivery records. It is rationale to consider that the two subpopulations examined constitute distinctive groups not only based on their religion but also on their way of living and biologic characteristics, as the genetic mixture between them is extremely rare.

The characteristics of the mothers who had congenitally malformed offspring and the infants who had major congenital malformations were studied. The presence of birth defects in the study population was determined by clinical examination and laboratory investigation which included chromosomal analysis when indicated and review of hospital or midwife referrals. The type of malformation was classified according to the organ system affected into central nervous system, cardiovascular, gastrointestinal, genitourinary, skeletal, multiple and chromosomal [1, 5].

The frequencies of major congenital malformations and other characteristics were compared between the two groups. The correlation between ethnicity and type of malformation, and the relative strength of association between various parameters (ethnicity, maternal age, gestational age at delivery, birthweight and type of major malformation) and perinatal mortality were also examined. Statistical analysis was performed using the chi-square test, t-test, binary and multinomial logistic regression analysis, and odds ratio (OR) and 95% confidence limits (CL) calculation. The statistical software package used was SPSS 10.0.

Results

From 1986 to 2001, among 10,027 deliveries in our department, 100 malformed infants were identified, accounting for a prevalence of 9.9 per 1,000 births. The proportions of Christian and Muslim mothers in the total number of deliveries were 59.8% (5,994) and 40.2% (4,028), respectively.

The age and parity of mothers, week at delivery, birthweight and sex (54% male) of malformed infants and perinatal mortality (67%) of all affected deliveries are presented in Table1. The above mentioned characteristics did not differ between the two ethnicities.

The prevalence of major congenital malformations was significantly higher in Muslims as compared to Christians (51/4028 (12.78%) vs 49/5994 (8.17%), p = 0.035).

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Table 1. — *Characteristics of the mothers and their infants in the total of malformed cases and in the two groups. Comparisons between the two groups by t-test and chi-square test showed no significant differences concerning each of these characteristics.*

	Total (n = 100)	Christians (n = 49)	Muslims (n = 51)
Age (years) (mean ± SEM)	26.45 ± 0.6	27.53 ± 0.77	25.41 ± 0.9
Parity (n) (mean ± SEM)	1.72 ± 0.09	1.73 ± 0.11	1.7 ± 0.14
Gestational age at delivery (weeks) (mean ± SEM)	34.86 ± 0.49	34.08 ± 0.73	35.6 ± 0.66
Birthweight (g) (mean ± SEM)	2294.79 ± 108.69	2077.23 ± 168.41	2495.29 ± 135.35
Sex (male) (n, %)	54 (54%)	23 (46.9%)	31 (60.8%)
Perinatal mortality (n, %)	67 (67%)	36 (73.5%)	31 (60.8%)

Table 2. — *The number and percentage in the respective number of deliveries (per 1,000) of various major congenital malformations in the two groups. Chi square was performed to compare the frequencies of these malformations in the total number of affected deliveries and in the total number of deliveries between the two groups.*

	Christians	Muslims	p
Cardiovascular	6 (1)	7 (1.74)	NS
Chromosomal	2 (0.33)	2 (0.49)	NS
CNS	17 (2.83)	18 (4.47)	NS
Gastrointestinal	8 (1.33)	8 (1.99)	NS
Genitourinary	1 (0.16)	0	NS
Lung	3 (0.5)	1 (0.24)	NS
Multiple	10 (1.7)	12 (2.97)	NS
Skeletal	2 (0.33)	3 (0.74)	NS
Total	49 (8.17)	51 (12.78)	0.035

NS = Non significant.

Table 2 shows the number of various malformations in the two groups. The frequencies of the various malformations in the total amount of affected deliveries did not differ significantly between the two groups. There were no significant differences when we compared each type of malformation in the total number of deliveries between the two groups. Furthermore, the comparison of the frequencies of each specific malformation (i.e. anencephaly, hydrocephalus, Down's syndrome, pyloric stenosis, etc.) between the two ethnicities showed no significant differences (data not shown). The prevalence of neural tube defects in the Muslim group (2.48%) was higher than in the Christian group (1.5%), although this difference did not attain statistical significance. Also, the prevalence of multiple major malformations was higher, although not significantly, in the Muslim group as compared to the Christian women (2.98% vs 1.67%).

Multinomial logistic regression analysis performed in the total of affected pregnancies showed that there was no dependency of the type of malformation from the ethnicity alone or controlled for maternal age, or even from the maternal age alone.

Figure 1 shows the incidence of major congenital anomalies throughout the examined time period in the two groups. Although there were no significant differences between the two groups for each year, an almost uniformly increased incidence in the Muslim population is obvious. As far as the incidence of major congenital anomalies within each ethnic group is concerned, the differences between their values for each year are not statistically different, although an increasing trend seems to exist during the examined years.

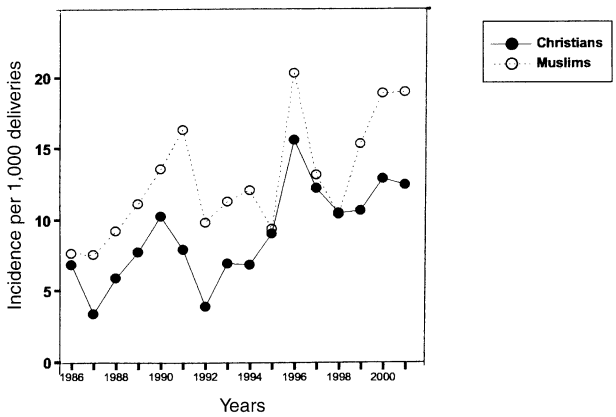

Figure 1. — Incidence of major congenital anomalies in the two groups: Thrace, Greece, 1986-2001.

Table 3 shows the frequencies of the various types of major malformations in the malformed stillbirths and early infant deaths (perinatal mortality). The perinatal mortality of babies with major congenital malformations was 6.68 per 1,000 births (67/10,027). In the total number of affected pregnancies binary logistic regression analysis showed that perinatal mortality depended significantly on CNS (OR 4.74, CL = 1.04-21.63, p = 0.044) gastrointestinal (OR 6.42, CL = 1.21-34.16, p = 0.029) and skeletal malformations (OR 61.38, CL = 3.82-985.37, p = 0.004) and gestational age at delivery (OR 1.24, CL = 1.07-1.42, p = 0.003; relative risk (RR) increases when gestational age decreases) but not on mother's ethnicity (OR 1.59, CL = 0.59-4.29, p = 0.361) and the other categories of major malformations. The adverse impact of preterm labor in the possibility of perinatal mortality in the affected pregnancies was also demonstrated when the gestational ages at delivery were compared between living malformed neonates and dead malformed cases. Of the total number of congenital malformations, but also in

Table 3. — *Number of cases and percentages of the various types of major congenital malformations in the malformed babies with perinatal mortality.*

Type of malformation	Number	Percent
CNS	23	34.3
Multiple	19	28.4
Cardiovascular	9	13.4
Gastrointestinal	8	11.9
Lung	4	6.0
Chromosomal	3	4.5
Skeletal	1	1.5
Total	67	100

the subgroups of Christians and Muslims, the gestational ages (mean ± SEM) at delivery of the cases with perinatal mortality were significantly lower than the living malformed neonates (33.8 ± 0.6 vs 37 ± 0.7, p = 0.02 and 33.1 ± 0.8 vs 36.7 ± 1.2, p = 0.031 and 34.5 ± 0.9 vs 37.3 ± 0.8, p = 0.045, respectively).

Discussion

The present study is the first in Greece that has examined the epidemiology of major congenital malformations as far as ethnicity is concerned.

A malformation is a primary error of normal development or morphogenesis of an organ or tissue. Malformations may be single or multiple and may be of minor or major clinical significance. About 14% of newborns have a single minor malformation, 3% of newborns have a single major malformation and 0.7% of newborns have multiple major malformations. There are various etiologies of major congenital malformations such as multifactorial inheritance (20%), monogenic (7.5%) and chromosomal disorders (6%), maternal illness (type I diabetes mellitus, epilepsy, phenylketonuria, etc.) (3%), congenital infection (2%), and drugs, radiation and alcohol abuse (1.5%); however, the majority of major congenital malformations are idiopathic (60%) [1]. Congenital malformations are a major cause of perinatal mortality and morbidity.

In the present study we did not examine the frequency of minor congenital malformations as they are of no clinical significance, although their existence should alert someone to the possibility of an associated major malformation which coexists in about 20% of infants with multiple minor malformations.

From our results, it is obvious that the prevalence of major congenital malformations is significantly higher in Muslim women as compared to the Christians. All types of malformations, except those regarding the lung and the genitourinary system accounted for this significant difference between the two ethnicities. However, when each type and specific major malformation were separately compared, the significance in differences was lost. This may be explained on the basis of the small numbers of cases that result after the subdivision into the various types and specific malformations.

The existence of ethnic differences in the incidence of lethal and non-lethal congenital malformations has been reported by various investigators [6-8]. Such increased incidence has been correlated to a combination of social, environmental and genetic factors [9]. Thus, this observation in babies of Asian origin was attributed to an excess of autosomal recessive disorders, which in many instances are the consequence of consanguineous relationships. Other studies in non-consanguineous populations have suggested that social and environmental factors (such as diet) may be influential [5, 9].

In the present study data about consanguinity and dietary habits were not available; however, in the future we will be able to get some relevant information as detailed questions about these issues are now included in the standard history obtained during the prenatal care of each pregnant. Nevertheless, based on our previous findings of less compliance of Muslim women in prenatal care guidelines (small number of prenatal visits, prenatal care initiation after 1st trimester and conclusively less adherence to prescribed medications during pregnancy) as well as a higher percentage of other adverse parameters like short inter-pregnancy interval [10], we could speculate that these women probably do not get an optimal amount and quality of nutrients (poorer baseline nutritional status). It would be possible that such a poor nutritional status, especially in the periconceptual period [11] could account for low dietary follic acid or zinc intake [12] and subsequently an increase in the incidence of neural tube defects. Therefore, this hypothesis remains to be confirmed with future adequately designed studies.

The significantly higher incidence of major congenital malformations in the Muslim group does not seem to result from a lesser degree of prenatal care provided to these women, mainly due to less adherence they exhibit to prenatal guidelines; this suggestion originates from the fact that standard prenatal diagnostic modalities (screening with biochemical markers and ultrasound examinations) are provided to each pregnant woman in our clinic irrespectively of her socioeconomic status and religion, and also that unpublished data showing that the greater proportion of congenital malformations detected and subsequently terminated were of Muslim women.

Another important finding of our study is the significant perinatal mortality observed in the malformed infants (67%) irrespectively of the ethnic origin (Christians 73.5% vs Muslims 60.8%, p = 0.256). However, in terms of absolute figures, perinatal mortality in Christians is higher than the respective in Muslims in the total number of malformed infants. But when we examined the cases with perinatal mortality attributed to major congenital malformations in the total number of deliveries, this was lower (6/1,000) in Christians than Muslims (7.6/1,000) (p = 0.357). Therefore, it is rationale to conclude that there are no differences in the perinatal mortality rate attributed to major congenital malformations between the two ethnicities. Central nervous system, multiple and congenital heart malformations were the most frequently associated with perinatal mortality, when the absolute figures are evaluated and this finding has also been observed in other populations [13]. However when a more sophisticated analysis was performed, examining the relative contribution of congenital anomaly, gestational age at delivery, birthweight, ethnicity and maternal age in malformed babies with perinatal mortality, then skeletal, gastrointestinal and CNS, but not multiple and congenital heart malformations were the most important determinants of this adverse perinatal outcome. The results of all the above-mentioned different methods of comparisons suggest that there are no differences in perinatal mortality between the two ethnic groups of malformed neonates.

The additional deteriorating impact of preterm labor in

perinatal mortality in the affected pregnancies which was demonstrated above is an expected finding.

It is also very important to stress that comparing our results with those from other countries [14-16] and also from another area in Greece, the incidence of major congenital malformations seems to be lower in the population of our area. Considering that a previous similar study in Greece [2] refers to data 30 years ago, we could speculate that the prevalence of these malformations has probably decreased during these periods in Greece. Although not demonstrable from the present study, one cannot exclude the possibility that developments in prenatal diagnoses may be important for such a historical reduction.

Conclusion

This is the first study in Greece showing that there is probably a higher prevalence of major congenital malformations in Muslims as compared to Christians, contributing to a sparse literature relevant to such epidemiologic issues. However, it can not elucidate whether increased risks among Muslims are related to potential underlying differences between the two ethnic groups. Further studies are required to clarify these issues and finally modify the risks in the Muslim population of this area in Greece.

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