The Impact of Prenatal Diagnosis and Termination of Pregnancy on the Relative Incidence of Malformations at Birth among Jews and Muslim Arabs in Israel*

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ABSTRACT: **Background:** Ultrasound examination of the fetus enables diagnosis of many major malformations during pregnancy, providing the possibility to consider termination of the pregnancy. As a result, in many cases the incidence of malformations at birth does not represent their true incidence.
Objectives: To determine the impact of prenatal diagnosis and pregnancy termination on the relative incidence of malformations at birth among Jews and Muslim Arabs in Israel.
Methods: Data on selected major malformations in 2000–2003 were collected from the two large central databases of the Ministry of Health and the Central Bureau of Statistics which contain information regarding births, stillbirths and terminations of pregnancies.
Results: For many malformations the total incidence was much higher than the incidence at birth. For almost all of the malformations studied, the total incidence was higher in Muslims than in Jews and the differences were further accentuated among the liveborn because of the differences in the rate of pregnancy terminations.
Conclusions: In order to detect possible influences of environmental or genetic factors on major malformations in Israel, it is critical to look at data including pregnancy terminations, stillbirths and live births.

IMAJ 2010; 12: 539–542

KEY WORDS: malformations, prenatal diagnosis, termination of pregnancy, Jews, Muslims

The population of Israel is estimated to be 7,282,000 and is both ethnically and religiously diverse. Jews constitute 80% of the population, while Muslims constitute 15%, Druze 3%, and Christians 2% [1]. Most of the Muslims and Christians are Arabs. There has been an impressive reduction in infant mortality rates among both Jewish and non-Jewish citizens since the creation of the State of Israel in 1948; however, differences remain particularly as a result of differences in the frequency of congenital malformations and genetic diseases [2]. Significant differences in the rate of malformations at birth between Jews and the Muslim and Druze populations were demonstrated in a study that used the National Registry of Birth Defects during the period 1991–2000 among more than 1.2 million liveborns [3]. However, since major fetal malformations may be diagnosed during pregnancy and often lead to pregnancy termination, the incidence at birth does not always represent the true incidence. The present study was performed to determine the impact of prenatal diagnosis on the rates of selected major malformations at birth among the two major religious communities in Israel – Jews and Muslims.

SUBJECTS AND METHODS

Data were collected from the two large central databases of the Ministry of Health and the Central Bureau of Statistics; these contain information on births, stillbirths and terminations of pregnancies. In Israel almost all infants are delivered in hospitals and the mandatory reporting of all live and stillbirths to the Ministry of Health includes details regarding the presence and type of congenital malformations. Since the year 2000, the mandatory report to the Central Bureau of Statistics of pregnancy termination for reasons of suspected fetal malformations includes details on the type of malformations diagnosed. These data are all coded according to the ICD-10 by a single coder and entered into the appropriate database. When the malformation is part of a syndrome, the code given is that of the syndrome.

Each of the two registries is linked to the Israeli Population Registry in which each liveborn is assigned a unique identification number and includes demographic details, among them religion. The Ministry of Health and the Central Bureau of Statistics registries were compared and duplicate entries were deleted. These consisted primarily of late terminations of pregnancy that are also registered as stillbirths. We report on the total number and rates of congenital malformations for live births, stillbirths and pregnancy terminations using the information from both registries after correcting for duplicates.

*** This article represents the opinions of the authors and not necessarily those of the Ministry of Health.**

Table 1. Selected malformations in the Israeli Jewish population between 2000 and 2003 among live births, termination of pregnancies and stillbirths

	Numbers of				Rates	
	Live births	TOP	Still births	Total	TOP/ Total	Total/ 10,000 LB
Abdominal wall defects	23	38	2	63	0.61	1.67
Anencephaly	17	154	17	188	0.82	4.99
Anophthalmia	2	2	1	5	0.4	0.13
Atresia esophagus	73	0	2	75	0	1.99
Atresia large intestine	82	1	3	86	0.01	2.28
Atresia small intestine	47	0	0	47	0	1.25
Choanal atresia	23	0	0	23	0	0.61
Cleft lip/palate	116	18	7	141	0.13	3.74
Cleft palate	90	6	1	97	0.06	2.58
Congenital kidney cystic disease	108	18	3	129	0.14	3.43
Diaphragmatic hernia	34	6	3	43	0.14	1.14
Encephalocele	8	25	3	36	0.69	0.96
Exstrophy bladder	5	0	0	5	0	0.13
Hypoplastic left heart	25	40	0	65	0.57	2.89
Prune belly syndrome	2	4	0	6	0.67	0.16
Reduction deformities of brain	7	21	6	34	0.62	0.9
Reduction deformities of limbs	62	17	0	79	0.22	2.1
Renal agenesis	96	27	4	127	0.21	3.37
Spina bifida	41	62	6	109	0.62	0.57
Tetralogy of Fallot	83	20	3	106	0.19	2.81
Transposition of great vessels	40	15	9	64	0.23	1.7
Trisomy 13 and 18	27	38	5	70	0.54	1.86
Trisomy 21*	358*	484		842	0.57	22.36

The stillbirths do not include late termination of pregnancy (Methods)

*A unique registry exists for trisomy 21 in the Ministry of Health and the numbers at birth include stillbirths.

TOP = termination of pregnancy

The rates of diagnosis of some of the malformations diagnosed at birth, such as congenital heart malformations, differ among the hospitals. In order to reduce this bias, we included in this study only malformations for which the diagnosis is unequivocal during pregnancy or at birth. Although this correction allows for greater uniformity, it is known that the registries are incomplete due to partial reporting and thus underestimate the rate of malformations in Israel.

Some of the information from these reports is not sufficiently specific due to the use of general terms such as "congenital heart malformations" or "multiple malformations," thus contributing further to an underestimation of the number of each malformation. In addition, when the malformations were part of a syndrome they were not included in the study. Since it is not always possible to differentiate in the report between unilateral and bilateral cases of major kidney malformations such as renal agenesis and congenital kidney disease, these malformations include both possibilities.

RESULTS

From 2000 to 2003 in Israel there were 376,627 liveborn Jewish infants and 144,625 liveborn Muslim Arab infants [1]. As expected, Down syndrome and open neural tube defects were the most frequent malformations among both Jews and Muslims [Tables 1 and 2]. For almost each of the malformations studied, the total incidence was higher in Muslims than in Jews [Table 3]. One exception was Down syndrome for which the total incidence among Jews (23.36 per 10,000 live births) was higher than among non-Jews (16.35 per 10,000 live births) as a direct consequence of the higher proportion of Jewish women being pregnant at later ages [1].

In addition, since for each of the malformations studied the rate of pregnancy termination was higher among Jews than among Muslims, almost all the malformations were more frequent at birth among Muslims than among Jews [Table 3]. For Down syndrome this resulted in a false impression that it is more frequent among non-Jews than in Jews.

For many of the malformations studied the rate at birth did not represent even an estimate of the true incidence. The most extreme example was anencephaly. Among Jews the rate of live births with anencephaly (0.45 /10,000 live births) was 10.9 times lower than its true incidence (4.99/10,000 live births).

DISCUSSION

From a public heath perspective, analysis of the relative incidence of malformations is important both for planning of services and for the determination of causal factors. In the case of the former, the rate of congenital malformations at birth is the variable that needs to be taken into account. However, in order to detect possible influences of environmental or genetic factors it is crucial to estimate the true incidence of the malformations. The true incidence must include data about terminations of pregnancy since the incidence at birth is strongly influenced by the rate of pregnancy termination for many of the malformations. In addition, since for some of the major malformations such as anencephaly many of the affected fetuses are stillborn, these data must also be added. Only the total rates of congenital malformations thus derived should be used to determine and follow the incidence of malformations in order to detect possible influences of environmental or genetic factors. The present study confirmed that in a country where termination

of pregnancy for malformations is possible, the incidence at birth is a very poor indicator of the true incidence for many of the malformations, and, as already noted, the most extreme example was anencephaly. As a result, while in some countries research on the rate of open neural tube defects at birth is enough to follow the implementation of food fortification with folic acid, in Israel such a study would not be representative. It would not have been possible to demonstrate the results of the 2000 recommendation for folic acid supplementation using only data from live births since no significant changes at birth were observed. Only with data on termination of pregnancies and stillbirths was the reduction in the incidence of open neural tube defects in Israel demonstrated [4]. In contrast, for malformations that are rarely diagnosed during pregnancy – such as cleft palate, choanal atresia or small intestinal atresia – incidence rates at birth are similar to the true incidence in the population.

In the present study the differences in the rate of pregnancy termination between Jews and Muslims were evident. The differences were present both for a severe and lethal malformation such as anencephaly (82% terminated among Jews and 60% among Muslims) and less severe malformations such as spina bifida (62% and 32%) or Down syndrome (57% and 24%). While among Jews more than 50% of pregnancies were terminated for 9 of the 23 selected malformations, among Muslims anencephaly was the only malformation for which more than 50% of the cases were terminated. Among Jews the rate of pregnancy termination for malformations was less than 50%, either because the malformation was difficult to diagnose or because the malformation itself was relatively mild. In the case of severe malformations such as renal agenesis and cystic malformations of the kidneys, it is probable that the relatively low rates of pregnancy termination are due to the inclusion of cases with unilateral malformations that allow for normal life. In contrast, among Muslims the pregnancies with a malformation were terminated for 16 of the 23 selected malformations in less than 10% of the cases.

What are the reasons for the difference in the rates of pregnancy termination for malformations in these two populations? Among the malformations that are diagnosed during pregnancy the differences in the rate of pregnancy termination between the two religious communities are mostly due to differences in religiosity [5]. According to Jewish Law, interruption of pregnancy is mostly forbidden after 40 days of pregnancy, whereas Islamic Law absolutely forbids termination of pregnancy after the 120th day of pregnancy. However, among Jews the majority of the population is secular and considers termination of pregnancy legitimate. As a result, as seen in the present study, for the most severe malformations the rates of termination of pregnancy are within a similar range (between 69% and 54%). On the other hand, the general Muslim population is traditionally religious, and the birth of a malformed child is often accepted as God's will and an event that should not be interfered with. Indeed, the rates of pregnancy termination are relatively low even for severe malformations.

Table 2. Selected malformations in the Israeli Muslim Arab population between 2000 and 2003 among live births, termination of pregnancies and stillbirths

	Numbers of				Rates	
	Live births	TOP	Stillbirths	Total	TOP/ Total	Total/ 10,000 LB
Abdominal wall defects	11	10	1	22	0.45	1.52
Anencephaly	17	76	34	127	0.6	8.78
Anophthalmia	2	0	0	2	0	0.14
Atresia esophagus	45	1	1	47	0.02	3.25
Atresia of large intestine	48	0	1	49	0	3.39
Atresia of small intestine	33	0	0	33	0	2.28
Choanal atresia	11	0	0	11	0	0.76
Cleft lip/palate	83	6	0	89	0.07	6.15
Cleft palate	39	1	1	41	0.02	2.83
Congenital kidney cystic disease	63	9	6	78	0.12	5.39
Diaphragmatic hernia	31	2	0	33	0.06	2.28
Encephalocele	16	6	4	26	0.23	1.8
Exstrophy bladder	3	0	1	4	0	0.28
Hypoplastic left heart	27	4	0	31	0.13	2.14
Prune belly syndrome	3	0	0	3	0	0.21
Reduction deformities of brain	10	4	2	16	0.25	1.1
Reduction deformities of limbs	43	5	1	49	0.1	3.39
Renal agenesis	29	3	3	35	0.09	2.42
Spina bifida	66	32	3	101	0.32	6.98
Tetralogy of Fallot	52	3	1	56	0.05	3.87
Transposition of great vessels	39	1	0	40	0.02	2.77
Trisomy 13 And 18	8	5	3	16	0.31	1.11
Trisomy 21*	179	57		236	0.24	16.35

The stillbirths do not include late termination of pregnancy (methods)

The data for trisomy 21 are obtained through a different registry for the non-Jewish population and the numbers at birth include stillbirths

TOP = termination of pregnancy

However, an important question that must be addressed but cannot be resolved by the present study is whether the differences in the rate of pregnancy termination represent only a difference in the approach to pregnancy or are also due to differences in the ability to arrive at a diagnosis during pregnancy. In the example of anencephaly, since almost all the cases are diagnosed during pregnancy, the differences in the rate of termination among the two groups are mainly explained by differences concerning the approach to termination. However, for other disorders such as cardiac malformations the ability to reach a prenatal diagnosis depends on the

Table 3. Selected malformations in the Israeli population between 2000 and 2003: comparison of the rates at birth and total rates between Jews and Arab Muslims*

	Live births rates			Total rates		
	Muslims	Jews	M/J ratio	Muslims	Jews	M/J ratio
Anencephaly	1.18	0.45	2.6 (1.3–5.1)	8.78	4.99	1.8 (1.4–2.2)
Atresia esophagus	3.11	1.94	1.6 (1.1–2.3)	3.25	1.99	1.6 (1.1–2.4)
Atresia large intestine	3.31	2.18	1.5 (1.1–2.2)	3.39	2.28	1.5 (1.0–2.1)
Atresia small intestine	2.28	1.25	1.8 (1.2–2.9)	2.28	1.25	1.8 (1.2–2.9)
Cleft lip/palate	5.74	3.08	1.9 (1.4–2.5)	6.15	3.74	1.6 (1.3–2.1)
Cleft palate	2.70	2.39	1.1 (0.8–1.6)	2.83	2.58	1.1 (0.8–1.6)
Congenital kidney cystic disease	4.36	2.87	1.5 (1.1–2.1)	5.39	3.43	1.6 (1.2–2.1)
Diaphragmatic hernia	2.14	0.90	2.4 (1.5–3.9)	2.28	1.14	2.0 (1.3–3.5)
Encephalocele	1.10	0.21	5.2 (2.2–12.2)	1.80	0.96	1.9 (1.1–3.1)
Abdominal wall defects	0.76	0.61	1.2 (0.6–2.6)	1.52	1.67	0.9 (0.6–1.5)
Hypoplastic left heart	1.87	0.66	2.8 (1.6–4.9)	2.14	1.73	1.2 (0.8–1.9)
Reduction deformities of brain	0.69	0.19	3.7 (1.4–9.8)	1.10	0.90	1.2 (0.7–2.2)
Reduction deformities of limbs	2.97	1.65	1.8 (1.2–2.7)	3.39	2.10	1.6 (1.3–2.3)
Renal agenesis	2.01	2.55	0.8 (0.5–1.2)	2.42	3.37	0.7 (0.5–1.0)
Spina bifida	4.56	1.09	4.2 (2.8–6.2)	6.98	2.89	2.4 (1.8–3.2)
Tetralogy of Fallot	3.60	2.20	1.6 (1.2–2.3)	3.87	2.81	1.4 (1.0–1.9)
Transposition of great vessels	2.70	1.06	2.5 (1.6–4.0)	2.77	1.70	1.6 (1.1–2.4)
Trisomy 13 and 18	0.55	0.72	0.8 (0.4–1.7)	1.11	1.86	0.6 (04–1.0)
Trisomy 21	1.23	0.92	1.3 (1.1–1.6)	16.35	22.36	0.7 (0.6–0.8)

*Includes only those malformations in which there were more than 5 cases among either Jews or Muslims

type of examination that was performed during pregnancy. Therefore, it is probable that at least some of the differences observed for malformations such as hypoplastic left heart (62% terminated among Jews and 13% among Muslims) or transposition of great vessels (23% and 2%) are secondary to differences of either availability or use of the medical services between the two populations.

In conclusion, when looking at the rate of malformations in a country such as Israel where interruption of pregnancy is allowed, it is critical to look at data including pregnancy terminations, stillbirths and live births to detect possible influences of environmental or genetic factors on major malformations.

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