MAJOR MALFORMATIONS DETECTED IN PALESTINIAN NEWBORNS HOSPITAL BASED STUDY

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GENERAL OVERVIEW

The frequencies of malformations vary among different ethnic groups. In addition some of these malformations as neural tube defects are known to exhibit secular variations.

The present study was undertaken to give preliminary data about the incidence of major malformations, detected at birth, among Palestinian population living in East Jerusalem and the southern part of the West Bank.

POPULATIONS AND METHODS

All cases of major malformations among deliveries of more than 500gms or 22 weeks of gestation whether they were a product of abortion, therapeutic termination, still born, or a live born were included. Mothers' data included age, parity, area, gestational age, obstetrical history and consanguinity.

DIAGNOSIS

Diagnosis of cases was based on the following:

1- Antenatal clinical and ultrasonic findings stated on admission, before delivery, as part of systematic examination or during regular antenatal care.

2- Clinical examination at birth, during the first week of life and in some cases (hospitalization in the neonatal unit) up to six weeks.

3- Postnatal brain, abdomen, renal, cardiac ultrasound examinations, axial computerized tomography and plain roentgenograms.

4- Autopsy was authorized in few cases by the family.

5- In cases of suspected intrauterine infection like hydrocephaly and microcephaly, non-immune hydrops, mother and baby serums were tested for evidence of toxoplasmosis and cytomegalovirus.

6- Metabolic workup and chromosomal studies were done upon clinical indications.

GLOBAL RESULTS

Between 1.1.1986 and 31.12.1995, 33969 newborns were registered at Makassed Hospital. Table I details these newborns regarding their status at birth, weight, early neonatal deaths and the number of deaths caused by malformations.

The number of stillborn recorded in this series was 730 (2.15% of total deliveries), among them 156 (21 %) had a severe congenital anomaly which could explain their death. Eight hundred twenty eight newborns died during the first 28 days of life (2.47% of total deliveries), 306 (37%) of these deaths were due to severe malformations.

The total number of perinatal deaths in this series (>22 weeks gestational age or >500 gm.) was 1558 (4.57 % of total deliveries), 462 had major malformations (29.6%).

The distribution of all newborns according to weight, status at birth and outcome is given in Table II. Table III details the number of normal and malformed newborns according to years. The outcome of malformed newborns is detailed as total, dead in the delivery room before admission to the neonatal unit, admitted to the neonatal unit and number of neonatal deaths. About 47% of malformed live newborns died in the neonatal period.

Table I
DISTRIBUTION OF NEWBORNS ACCORDING TO WEIGHT

WEIGHT	LB	SB		TB	END		ND		PND	
	N	N	CA	N	N	CA	N	CA	N	CA
<500	5	8	0	13	5	0	5	0	13	0
501-750	128	96	15	224	121	7	128	7	224	22
751-1000	203	98	17	301	145	20	152	20	250	37
1001-1250	332	55	12	387	97	28	136	29	191	41
1251-1500	439	67	16	506	78	25	102	32	169	48
1501-1750	488	35	8	523	42	35	49	25	84	33
1751-2000	678	47	13	725	39	27	48	30	95	43
2001-2250	998	44	12	1042	35	30	39	31	83	43
2251-2500	1622	43	12	1665	19	17	29	23	72	35
>2500	26709	195	44	26904	107	79	133	105	328	149
>4000	1637	42	7	1679	5	3	7	4	49	11
Total	33239	730	156	33969	693	271	828	306	1558	462

LB: Alive born, SB: Stillborn, TB: Total born, ND: Neonatal deaths, END: Early neonatal deaths, N: number, CA: Congenital anomaly, PND: perinatal deaths.

Table II
DISTRIBUTION OF NEWBORNS ACCORDING TO YEAR AND OUTCOME

Y	**TB**	**SB**		**LB**	**LB-CA**					**PND**
		N	**CA**	**N**	**T**	**DDR**	**ADNU**	**END**	**ND**	**CA**
86	2021	45	8	1976	31	0	31	17	19	27
87	2060	58	13	2002	45	3	42	18	22	35
88	2633	51	14	2582	66	3	63	26	32	46
89	3959	104	30	3855	48	8	40	23	26	56
90	4327	117	26	4210	70	2	68	34	41	67
91	3820	92	13	3728	61	8	53	35	38	51
92	4289	87	12	4202	82	10	72	42	44	56
93	3825	79	18	3746	70	10	60	27	29	47
94	3758	57	15	3701	98	6	92	34	38	53
95	3277	40	7	3237	85	1	84	15	17	24
T	**33969**	**730**	**156**	**33239**	**656**	**51**	**605**	**271**	**306**	**462**

LB: Alive born, SB: Stillborn, TB: Total born, ND: Neonatal deaths, END: Early neonatal deaths, N: number, CA: Congenital anomaly, PND: perinatal deaths. T: Total, DDR: death in delivery room, ADNU: admission to neonatal unit

CLASSIFICATION OF MALFORMATIONS

During the studied period 812 newborns were detected with a single or multiple malformations, 449 were males and 363 were females.

Each malformed newborn was classified in one of the major categories. If other defined major malformations were present in the same patients they were described as associated ones. Priority in classification was considered first for chromosomal pathology then for major CNS malformations and third malformations according to their anatomical distribution. Classification within each anatomical system will be detailed in related chapters. Patients with multiple congenital malformations were classified in known defined syndrome whenever possible or kept in the category of MCA when they could not be fitted in a described syndrome.

Table III
DISTRIBUTION OF MALFORMED NEWBORNS IN MAJOR CATEGORIES

MALFORMATION	M	F	T	SB	ND	M/1000 DEL	1M /XDEL
All CNS	149	160	309	104	151	9.1	110
-NTD	77	99	176	62	100	5.18	193
-Other CNS	72	61	133	42	51	3.92	255
Uro-renal	53	32	85	7	23	2.50	400
Congenital Heart Diseases	37	30	67	1	21	1.97	507
Chromosomal aberrations	38	26	64	6	21	1.88	531
Skeletal malformations	35	26	61	6	35	1.76	557
G I malformations	31	21	52	1	5	1.54	653
Facial malformations	25	18	43	1	3	1.27	790
MCA-undefined + defined S	17	17	34	6	17	1.00	999
Non immune hydrops	17	10	27	22	4	0.79	1258
Metabolic diseases	15	12	27	1	13	0.79	1258
Thoracic defects	21	5	26	1	12	0.77	1307
Skin	11	6	17	0	1	0.50	1998
TOTALS	**449**	**363**	**812**	**156**	**306**	**23.90**	**41.83**

Table IV
OVERVIEW OF MALFORMED NEWBORNS BY ANOMALY

MALFORMATION	M	F	T	SB	ND	M/ 1000DEL	M/DEL
Hydrocephaly	64	48	112	42	44	3.30	303
Anencephaly	31	39	70	37	33	2.06	485
Myelomeningocele	30	40	70	14	42	2.06	485
Trisomy 21	30	9	39	1	3	1.15	871
Hydronephrosis	25	13	38	2	0	1.12	894
Non Cyanotic CHD	15	12	27	0	6	0.79	1258
Non immune hydrops	17	10	27	22	4	0.79	1258
Metabolic diseases	15	12	27	1	13	0.79	1258
MCA-undefined S	15	11	26	5	13	0.77	1307
Arthrogryposis	11	14	25	3	21	0.74	1359
Diaphragmatic Hernia	18	4	22	1	9	0.65	1544
Meckel-Gruber S.	8	10	18	6	12	0.53	1887
Cyanotic heart disease	10	7	17	1	11	0.50	1998
Tracheo-oesophageal fistula	8	9	17	0	2	0.50	1998
Encephalocele	7	9	16	5	11	0.47	2123
Cleft Lip Palate	11	3	14	1	0	0.41	2426
Myocardiopathy	6	7	13	0	3	0.38	2613
Imperforate anus	7	6	13	0	0	0.38	2613
Icthyosis	8	5	13	0	1	0.38	2613
Intestinal Atresia	6	5	11	0	1	0.32	3088
Microcephaly	4	6	10	0	3	0.29	3397
Dextrocardia	6	4	10	0	1	0.29	3397
Ambiguous genitalia	5	4	9	0	0	0.26	3774
Renal agenesis	7	2	9	1	8	0.26	3774
Cleft Palate	5	4	9	0	0	0.26	3774
Polycystic kidney	3	5	8	1	7	0.24	4246
Defined Syndromes	2	6	8	1	4	0.24	4246

Table IV
OVERVIEW OF MALFORMED NEWBORNS BY ANOMALY (cont.)

MALFORMATION	M	F	T	SB	ND	M/ 1000DEL	M/DEL
Craniostenosis	3	4	7	0	0	0.21	4853
Trisomy 13	3	4	7	0	7	0.21	4853
Trisomy 18	2	5	7	0	7	0.21	4853
Dysplastic, hypoplastic kidneys	4	3	7	0	5	0.21	4853
Other skeletal anomalies	4	3	7	0	0	0.21	4853
Pierre Robin	2	5	7	0	2	0.21	4853
Turner	0	6	6	5	0	0.18	5662
Camptomelic dysplasia	4	2	6	0	5	0.18	5662
Thanatophoric dysplasia	1	5	6	2	4	0.18	5662
Prune Belly	3	2	5	0	3	0.15	6794
Post urethral valve	5	0	5	1	0	0.15	6794
Macrosomia	5	0	5	0	1	0.15	6794
Hirchsprung disease	5	0	5	0	1	0.15	6794
Cleft lip +	2	3	5	0	0	0.15	6794
Osteogenesis Imperfecta	4	0	4	1	0	0.12	8492
Hyperlaxity syndromes	4	0	4	0	1	0.12	8492
Epidermolysis Bullosa	3	1	4	0	0	0.12	8492
Noonan	3	0	3	0	2	0.09	11323
Multicystic kidney	1	2	3	2	0	0.09	11323
Goldenhar	1	2	3	0	0	0.09	11323
Lung malformation	3	0	3	0	2	0.09	11323
Iniencephaly	1	1	2	0	2	0.06	16985
Hydranencephaly	1	1	2	0	2	0.06	16985
Caudal Regression	0	2	2	0	2	0.06	16985
Klippel Feil	0	2	2	0	1	0.06	16985
Achondrogenesis	2	0	2	0	2	0.06	16985
Omphalocele	2	0	2	0	0	0.06	16985
Gastroschisis	1	1	2	1	0	0.06	16985
Choanal atresia	1	1	2	0	0	0.06	16985

Table IV
OVERVIEW OF MALFORMED NEWBORNS BY ANOMALY (cont.)

MALFORMATION	M	F	T	SB	ND	M/ 1000DEL	M/DEL
Translocation P4-7	0	1	1	0	1	0.03	33969
44 Del 18(ptr)	0	1	1	0	1	0.03	33969
Nephrotic syndrome	0	1	1	0	0	0.03	33969
Choledocal Cyst	1	0	1	0	0	0.03	33969
Mesenteric cyst +	1	0	1	0	1	0.03	33969
Agnathia, isolated	1	0	1	0	1	0.03	33969
Tracheal atresia	0	1	1	0	1	0.03	33969
TOTAL	**449**	**363**	**812**	**156**	**306**	**23.90**	**42**

DISCUSSION

A number of surveys have indicated that globally at least 2 per 1000 neonates have autosomal recessive disorders, 2-10 per 1000 have autosomal dominant disorders, 1-2 per 1000 have X-linked recessive disorders, 6-7 per 1000 have chromosomal abnormalities and about 20 per 1000 have congenital malformations [1]. A recent publication on genetic disorders among Arab populations lists 115 new genetic syndromes reported over the past two decades. Of these, 100 syndromes are autosomal recessive, 10 are autosomal dominant and 5 possibly X-linked recessive or autosomal recessive [2].

Birth defects arise at the time of conception or during intrauterine development. The frequency of inherited and congenital anomalies varies widely, from 1%-10% of live births if all minor defects are included [3]. Major congenital anomalies (MCAs) are the leading cause of perinatal and infant morbidity and mortality in industrialized and developing countries. The number of epidemiological studies of congenital anomalies in the Arab population is increasing denoting the importance of the question [4,5,6,7,8,9,10,11,12,13,14,15] .

The best and comprehensive method for investigating birth defects is a review of hospital maternity records for all births. Such method can generate information on the magnitude of birth defects, their pattern and associated risk factors and for planning or designing appropriate preventive, therapeutic and rehabilitative programs. In our condition at the time of the study this approach was not possible for political and technical reasons.

The classification of malformations and their severity was to some extent similar to that used by Christianson et al. (16). We have preferred to base our study on malformed babies and not on individual malformation. It is a well known fact that many malformed babies have multiple and complex malformation. For a first global study reported on this population we have preferred the baby approach and not the individual malformation one. Malformations were classed as minor when they affected non-vital organs, had little or no functional effect and did not cause distress in the neonatal period. They were classed as major when they were potentially life-threatening and, if not corrected, would impair the child's development or well-being. Congenital hip dislocation suspected at birth was not considered for example as a major one in this study.

This study is a hospital-based survey; the data might not be a good reflection of the incidence of congenital anomalies in this population, the large number included in this series is a possible correcting factor among others. At the time where the study took place there were not yet established programs for prenatal detection or termination of malformed babies. Major congenital anomalies constituted 38% of all cases with malformations. Out of a total of 730 stillbirths, 156 (21%) had congenital anomalies, as did 306 (37%) out of 828 neonatal deaths. This underlines the significant contribution made by congenital anomalies to neonatal mortality and morbidity in this population.

The methodology of this study can not allow easy comparisons with data reported in Arab countries and more details will be given when reporting results of particular malformations.

Table V compare selected malformations prevalence found in this study with the WABD results and some striking increase in the rate of CNS malformations was noticed.

The prevalence of 23.9 per 1000 births is high and can be compared to studies in the United Arab Emirates (UAE) and Saudi Arabia [6, 7, and 8]. Temporal, geographical and racial variations in the magnitude of congenital anomalies reported in addition to variations in case ascertainment complicates further the task of comparison. Longitudinal observations have shown fluctuations in the frequency of congenital anomalies over time. For instance, congenital anomalies in Bahrain increased from 7.2 to 18.7 per 1000 live births between 1978 and 1985 [9] and anencephaly in Kuwait declined from 3.2 to 1.3 per 1000 births between the 1970s and 1980s.[10]

Table V
RATE OF SELECTED MALFORMATIONS AND COMPARISON WITH WABD

Malformation	TX	SB	ND	M/10000 Total B	M/10000 Live B	WABD
Anencephaly	70	37	33	20.61	9.94	4.8
Myelomeningocele	70	14	42	20.61	16.86	6.2
Encephalocele +Meckel-Gruber	34	11	11	10.01	6.93	1.3
Hydrocephaly	112	42	44	32.97	21.08	5.6
Microcephaly	10	0	3	2.94	3.01	2
Polycystic kidney +Renal agenesis	17	1	7	5.00	4.82	5
Trisomy 21	39	1	3	11.48	11.44	14.5
Trisomy 18	7	0	7	2.06	2.11	2.9
TEF	17	0	2	5.00	5.12	2.6
Small intestinal atresia	10	0	1	2.94	3.01	1.9
Omphalocele+gastroschisis+Prune-Belly	9	1	0	2.65	2.41	4
Cleft lip palate	14	1	0	4.12	3.91	10.2
Cleft palate +Pierre Robin	11	0	0	3.24	3.31	5.4
Diaphragmatic hernia	22	1	9	6.48	6.32	2.9

***WABD**: World Atlas of Birth defects 1988(Results given for live births)*

Live births with congenital anomalies were found to have high rates of perinatal death in the UAE (36%) and Saudi Arabia (37%) [6,7,8,12]. We observed fatality rates due to congenital anomalies close to those observed in the UAE and Saudi Arabia (37%) and lower than in Libya (49.1%) [17].

The frequency of cardiovascular malformations was lower than expected probably because of a low level of clinical detection and lack of routine ultrasonography in the neonatal period and absence of routine autopsy. Throughout the world, chromosomal aberrations are among the least defined causes of congenital anomalies and cognitive defects. These disorders constitute a significant proportion of the genetic problems of the Eastern Mediterranean Region, giving rise to congenital abnormalities in about 5 per 1000 live births [5]. The incidence of trisomy-21 was also lower than that shown in the literature (1.15 per 1000). As not all congenital anomalies were systematically karyotyped, it is possible that the true incidence of chromosomal disorders was underestimated in our study but comparable low rates were also reported in other populations. The incidence of Down syndrome per 1000 live births in this study was lower than the 2.2 per 1000 reported in Benghazi, [17], comparable to the 1.14 per 1000 in Bahrain, and less than the 1.8 per 1000 in Saudi Arabia [13].

The consanguinity rate in this study was 57% but we have not extended comparisons between product of consanguineous and non consanguineous couples in this study. This important factor needs a well designed prospective study in the near future.
The inherited hematological disorders and routinely screened endocrine and inborn errors of metabolism were not the subject of this study, as most are autosomal recessively inherited, except 27 cases detected at birth and most of them were admitted to the neonatal ICU for workup including internal or CNS malformations. The incidence of autosomal recessive diseases would be expected to be higher with consanguineous marriages and some other congenital anomalies that manifest after the neonatal period, such as various heart defects, are surely underestimated in this series.

Socioeconomic factors as influencing the risk of malformations were not studied in this series. The majority of the population studied is of lower and middle social classes and the national income per capita is less than 1000 USD/year. Some studies have concluded that more deprived populations have a higher risk of congenital anomalies of non-chromosomal origin and cardiac malformations but not neural tube defects [18].

Males represented 53% of the malformed newborns (and 51 of the all newborns). This mild predominance was not found in CNS malformations where females were more predominant in contrast with results published in a population based study [19].

Never the less, this study provides a framework to anticipate and plan services for the prevention and treatment of some congenital anomalies in this population. Antenatal diagnosis and counseling is available for some of these anomalies, but customs, beliefs, cultural and religious factors are to be taken into consideration in addition to medical aspect.

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