MALTA CONGENITAL ANOMALIES REGISTER

HALF YEARLY REPORT JULY - DECEMBER 1997

SURVEILLANCE OF CONGENITAL ANOMALIES

Widespread interest in the epidemiology of birth defects started in the 1960's, when many countries had been affected by the increasing number of babies born with limb defects following the use of thalidomide as a sedative in early pregnancy between 1958 and 1962[1]. Since then, several countries have established systems for surveillance of anomalies.

As the prevalence of anomalies is relatively low, many births need to be surveyed before trends and differences in rates can be reliably identified. To increase the numbers observed international collaboration has been developed.

International Clearing House Of Birth Defects Monitoring Systems (ICBDMS).

In 1974, representatives from many data collecting systems in Europe, America and Australia met in Helsinki and agreed to work towards a regular exchange of data. This led to the establishment of the International Clearinghouse of Birth Defects Monitoring System (ICBDMS)[2]. An International Centre for ICBDMS is presently based in Rome.

The objectives of the ICDBMS are ' to provide for rapid communication of information among various birth defects monitoring or surveillance programmes around the world' and to ' prevent birth defects'[3]

In 1996, there were 26 participating programmes in ICDBMS. Altogether they cover over 2.5 million births per year. To be considered a full member of the Clearinghouse, a programme must have an established baseline and monitor a minimum of 20,000 births annually. Associate members monitor at least 5,000 births annually.

There are no standard guidelines as to methodology of data collection nor are there consistent definitions as to ' stillbirth' . Laws regarding termination of pregnancy are different and accessibility to data on termination of pregnancy varies between the programmes. Some programmes are population based, others hospital based. Some are mandated by law, others are not. This diversity makes it difficult to compare rates between the different participating programmes. The Clearinghouse instead focuses on following trends in prevalence of various anomalies within the same country over a period of years. For purposes of the ICBDMS, only data on birth defects diagnosed at birth or in the perinatal period are included. Besides issuing annual reports, a major function of the ICBDMS is collaborative research.

EUROCAT (European Registration Of Congenital Anomalies and Twins)

EUROCAT is an Association of Congenital Anomalies Registries within Europe. It was conceived in 1974 when the Committee on Medical and Public Health Research of the EEC felt the need of having collaborative epidemiological surveillance systems between countries of the EEC[1]. EUROCAT was consequently initiated in 1979. The long term objective of EUROCAT was to test the feasibility of and encourage collaboration between European countries in the collection, analysis and interpretation of data taking congenital anomalies as an example. It would provide guidelines for conformity in surveillance and a Central Registry which could process data from the participating countries [4]. The specific objectives of EUROCAT were

- to provide baseline epidemiologic information on congenital anomalies in Europe;
- to detect and investigate trends in their frequency;
- to evaluate the effectiveness and efficiency of health services;
- to provide a database for research and to act as an information centre.

Registration of anomalies started in 1979 in 9 centres from 5 European countries. These have increased to 31 centres in 15 countries in 1997. Malta has been a member of EUROCAT since 1986.

EUROCAT registries follow standardised guidelines, employ multiple sources of case ascertainment and use validation and identification systems to avoid duplicate registrations. They include all infants/fetal deaths with anomalies diagnosed until 1 year of life. The criteria which must be met by registries

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participating in EUROCAT include the definition of population, coverage of fetal deaths and induced abortions, data collection and ascertainment, definition and coding of defects, calculation of prevalence rates and confidentiality[4]. In this way comparison between prevalence data is possible.

References:

1 Weatherall JAC. The Beginnings of EUROCAT. Belgium, Louvain la Neuve, 1985; p8.

2 Weatherall JAC. Surveillance of congenital malformations and birth defects. In Surveillance in health and disease. Eylenbosch WJ, ND Noah (eds) Oxford University Press Oxford 1988; pp 100-114.

3 International Clearinghouse for birth defects monitoring systems. Annual Report 1996 with data for 1994. International Centre for birth defects, Rome, 1996; pp 5-45.

4 Lechat MF. European registration of congenital anomalies. In Epidemiology; Biochemical and Health research. Vuylsteek K, Hallen M. (eds), Netherlands, IOS Press, 1994; pp 57-72.

TRISOMY 18 (EDWARD SYNDROME)

During 1997 there were 4 cases of trisomy 18 reported, 2 males and 2 females. All were livebirths but 3 died within the first week of life. Two were confirmed by genetic studies, while two died before these studies were performed. One female is still alive (April 1998) at one year of age. None of these babies were diagnosed prenatally.

Edward syndrome (Trisomy 18) is characterised by a specific clinical pattern of abnormalities including prominent occiput, abnormally shaped ears, micrognathia, short sternum, narrow pelvis, clenched hand and overlapping fingers, rocker bottom feet, mental and developmental disability. The syndrome is associated with life threatening malformations such as cardiac defects, congenital diaphragmatic hernia and oesophageal atresia. Life expectancy is limited; 30% of patients die within the first month of life while only 10% survive beyond one year [1]. More recent studies suggest that survival may be even less than this. The lower survival rates reported recently may be explained by earlier diagnosis; such that affected babies who would have died prior to detection in earlier times are now diagnosed and documented[2].

Trisomy 18 is the second most common trisomy after trisomy 21. It occurs most frequently as a ' free' trisomy and more rarely as a translocation trisomy or mosaic. The syndrome is typically associated with duplication of the entire chromosome 18, however, several individuals have been reported with partial trisomies of chromosome 18[3]. Individuals with only partial trisomy 18 display a range of clinical severity from the relatively mild phenotype with no internal organ malformations to the classical characteristics of Edward syndrome, depending on which portion of chromosome 18 is triplicated[3].

The EUROCAT average prevalence rate for Edward syndrome is given as 3.3 per 10000 births, that is, approximately 1 in 3000 births[4]. The prevalence of Trisomy 18 in all clinically recognised pregnancies is significantly greater than that in newborns[5], implying that many conceptuses with trisomy 18 do not survive to birth.

Similar to other chromosomal anomalies, the occurrence of trisomy 18 is related to parental age, such that increased maternal and paternal age is associated with increased risk of the abnormality. The parental origin of the extra chromosome 18 has been assessed in several studies, and it is reported that in about 85% of cases it is of maternal origin[5].

Both prenatal and livebirth sex ratios show an excess of females with the condition. This difference is more marked in the livebirth sex ratios, implying that there is a significant selection pressure against males in the prenatal period[6]. Females are also reported to live longer than males[2].

Edward syndrome may be detected antenatally by prenatal screening which includes a combination of ultrasonography, maternal serum tests and amniocentesis. Termination of pregnancy may be offered in countries where this is legal. Intrauterine growth retardation, and polyhydramnios are often found in pregnancies with trisomy 18[7,8]. A significant proportion are delivered by caesarean section, the main reasons being fetal distress and intrauterine growth retardation[8].

Most infants with Edward syndrome have a very short life expectancy and all survivors have severe mental retardation. Practically all die before 10 years of age, although there are individual case reports of children surviving into their teenage years[2]. A postnatal diagnosis of Edward syndrome is therefore associated with difficult medical and ethical issues regarding whether or not to institute aggressive treatment in a newborn with trisomy 18 and a life threatening anomaly[9].

Although survivors function in the severe to profound developmentally handicapped range they do achieve some skills of childhood and always continue to learn. Older children can learn to use a walker, understand words and phrases, use a few words and/or signs, crawl, follow simple commands, recognise and interact with others, and play independently. Thus the child with trisomy 18 may interact with his or her environment and family during their limited lifespan[8].

In Malta and Gozo, during 1993-1996 there were 5 cases (2 males, 3 females) of Edward syndrome reported, giving a prevalence rate of 2.5 per 10000 births. Two died within the first week of life. The average maternal age at delivery was 33.6 years which is significantly higher than that of the general population (29.2 years). None of the cases were diagnosed prenatally.

References:

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4. EUROCAT Working group. 15 years of surveillance of congenital anomalies in Europe 1980-1994 EUROCAT Report 7. Belgium, Scientific Institute of Public Health Louis Pasteur, 1997 pp 10-149.
5. Ya-gang X. et al. Parental origin of the supernumerary chromosome in trisomy 18. Clin. Genet. 1993; 44: 57-61
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This report includes all reported major anomalies diagnosed from July - December 1997.

Total number of infants/fetuses diagnosed with congenital anomaly

Hospital		Total births*		With Congenital anomaly	
		Livebirths	Fetal Deaths	Livebirths	Fetal Deaths
St. Luke' s Hosp.	M	1031	6	32	1
	F	988	5	22	1
Gozo Gen. Hosp.	M	102	0	1	0
	F	98	0	1	0
Private Hosp.**	M	117	0	0	0
	F	114	1	2	0
Total		2450	12	58	2

*Provisional data from hospital records and death register.

**Private Hosp. include Capua Palace, St. James' and St. Philip' s

Distribution of infants/fetuses according to number of major anomalies

Anomalies	Number of Infants/fetuses
Single major anomaly	42
Two or more major anomalies of same system	5
Major anomalies involving two systems	4
Major anomalies involving three or more systems	2
Chromosomal anomalies	4
Multiple anomalies and other syndromes not elsewhere classified	3
Total	**60**

Distribution of infants/fetuses with congenital anomalies according to system/s involved

ICD code	System	Number of infants/fetuses			Fetal deaths
		Total	Males	Females	
7400-20	Neural tube defects	1	1	0	1
7421-29	Other nervous system defects	0	0	0	0
7430-49	Eyes, ears, face and neck	1	0	1	0
7450-79	Cardiovascular	26	12	14	0
7480-89	Respiratory	0	0	0	0
7490-93	Cleft palate and lip	2	2	0	0
7500-19	Upper alimentary tract	1	0	1	0
7520-29	Genital organs	3	3	0	0
7530-39	Urinary	3	2	1	0
7540-59	Musculoskeletal limbs & skull	6	4	2	0
7560-69	Other musculoskeletal defects	2	2	0	0
7570-79	Skin	2	1	1	0
7580-89	Chromosomal anomalies	4	3	1	0
7590-92	Endocrine glands	0	0	0	0
7593-96	Other anomalies	0	0	0	0
7597-99	Multiple anomalies/ Syndromes	3	1	2	1
	Two systems	4	2	2	0
	Three or more systems	2	1	1	0
	Total Infants with anomalies	**60**	**34**	**26**	**2**

	Anomalies grouped according to system involved	Total	Male	Female
7400-7420	**Neural Tube defects**	**2**	**1**	**1**
7400	Anencephaly	1	1	0
7412	Myelomeningocele	1	0	1
7421-7429	**Other anomalies of nervous system**	**4**	**2**	**2**
7422	Reduction deformities of brain	3	1	2
7424	Other specified anomalies of the brain	1	1	0
7430-7449	**Anomalies of the eye, ear, face and neck**	**1**	**0**	**1**
7430	Anophthalmos	1	0	1
7450-7479	**Anomalies of cardiovascular system**	**36**	**20**	**16**
7451	Discordant ventriculoarterial connection	1	1	0
7452	Tetralogy of Fallot	2	2	0
7453	Single ventricle	1	1	0
7454	Ventricular septal defect	12	6	6
7455	Atrial septal defect	13	3	10
7456	Endocardial cushion defect	1	1	0
7460	Anomalies of pulmonary valve	1	1	0
7470	Patent ductus arteriosus	2	2	0
7471	Coarctation of the aorta	1	1	0
7472	Other anomalies of aorta	2	2	0
7480-7489	**Anomalies of respiratory system**	**1**	**1**	**0**
7480	Anomalies of nose	1	1	0
7490-7493	**Cleft palate and cleft lip**	**4**	**3**	**1**
7490	Cleft of secondary palate	2	2	0
7492	Cleft of primary and secondary palate	2	1	1
7500-7509	**Anomalies of upper alimentary tract**	**1**	**0**	**1**
7513	Hirschprung' s disease	1	0	1
7510-7519	**Other anomalies of the digestive system**	**0**	**0**	**0**
7520-7529	**Anomalies of the genital organs system**	**5**	**5**	**0**
7525	Anomalies of testicles	1	1	0
7526	Hypospadias/epispadias	4	4	0
7530-7539	**Anomalies of the urinary system**	**6**	**4**	**2**
7532	Obstructive defects of renal pelvis and ureter	5	4	1
7533	Other specified anomalies of kidney	1	0	1
7540-7559	**Deformities of the musculoskeletal system**	**10**	**6**	**4**
7540	Cong. musculoskeletal deformities skull/face	1	0	1
7545	Varus deformities of feet	4	2	2
7547	Other deformities of feet	1	0	1
7550	Polydactyly/ polysyndactyly, hand & foot	2	2	0
7551	Syndactyly hand and foot	1	1	0
7558	Other specified anomalies of unspecified limb	1	1	0
7560-7569	**Other musculoskeletal anomalies**	**2**	**2**	**0**
7560	Anomalies of skull and face bones	1	1	0
7567	Anomalies of abdominal wall	1	1	0
7571-7579	**Congenital anomalies of the integuement**	**2**	**1**	**1**
7571	Icthyosis congenita	1	1	0
7573	Other specified anomalies of skin	1	0	1
7580-7589	**Chromosomal anomalies**	**4**	**3**	**1**
7580	Down syndrome	1	1	0
7582	Edward syndrome	3	2	1
7593-7599	**Other congenital anomalies**	**3**	**1**	**2**
7598	Other syndromes or associations	2	1	1
7599	Congenital anomaly not otherwise specified	1	0	1

NB - Spina bifida occulta is only registered when there are complications or when it occurs in combination with other major anomalies

- Hydrocephaly occurring with spina bifida is not included
- Glandular hypospadias is not recorded, unless in combination with other congenital anomalies