Birth defects in Singapore: 1994 - 2000

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ABSTRACT

Introduction: To study characteristics of birth defect cases among live births, stillbirths and abortions in Singapore between 1994 and 2000.

Methods: Index cases for the National Birth Defects Registry (NBDR) were obtained from all neonatal nurseries in Singapore, all hospital discharge summaries, cytogenetic and pathology reports from all pathology laboratories in Singapore, and from the compulsory reporting of all termination of pregnancy cases and stillbirths delivered. Further information was obtained from case notes retrieved from the medical record offices, antenatal clinics, cytogenetic laboratories, pathology departments and the Registry of Births and Deaths. The notified cases (live births, stillbirths and abortions) between 1994 and 2000 were extracted from the NBDR and analysed with regard to ethnicity, maternal age, trend over the seven years and types of birth defects using the British Paediatric Association Classification.

Results: Between 1994 and 2000, a total of 7,870 cases (6,278 births and 1,592 abortuses) were notified, giving a rate of 23.99 birth defect cases per 1000 live births. There was a decreasing trend in birth defect incidence (19.76 to 16.85 per 1,000 live births) among live births and stillbirths and an increasing trend of abortion (3.25 to 7.57 per 1,000 live births) for birth defects. Malays had a higher rate of congenital defects at birth (24.4/1,000 live births) compared to Chinese (18.4/1,000 births). The 25-29 years age group had the lowest overall rate (22.6/1,000 live births) compared to the 19 years and below group at 31.6/1,000 live births and the 45-49 years group at 126.6/1,000 live births. The five most common groups of anomalies (per 1,000 live births) were those of heart (9.07), musculoskeletal (4.98), chromosomal (4.35), urinary (3.12) and nervous systems (2.90). The five most common aborted anomalies (per 1,000 live births) were those of chromosomal (2.40), nervous (1.23), heart (0.95), musculoskeletal (0.85) and urinary systems (0.36).

Conclusion: There was an increasing trend of abortion for birth defects, accompanied by a falling trend in the congenital anomalies of live births. Both extremes of maternal age were at higher risk of non-chromosomal birth defects while advanced maternal age was at higher risk of chromosomal defects.

Keywords: abortion, birth defect, chromosome disorders, congenital abnormalities

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INTRODUCTION

Congenital birth defects have now become a major cause of perinatal and infant morbidity and mortality in Singapore. The National Birth Defects Registry (NBDR) was set up by the Ministry of Health on January 1, 1993 to gather data on congenital birth defects in Singapore. The registry collates information on a national scale and helps to facilitate the planning and evaluation of antenatal screening, genetic counselling and paediatric medical and surgical services. Since February 1, 1999, NBDR was transferred to and based at the KK Women's and Children's Hospital (KKH). This paper aims to study characteristics of birth defects cases among live births, stillbirths and abortions in Singapore between 1994 and 2000.

METHODS

The method of data collection of NBDR has previously been described[1]. To summarise, data collection was based on multiple sources comprising government bodies, public and private medical centres. These included the Health Regulation (HR) Division and the Epidemiology & Disease Control (E&DC) Division of the Ministry of Health, the National Registry of Births and Deaths (RBD)

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Table I. Exclusion list.

Abnormal palmer crease	Limbs – one smaller than other
Absent abnormal fontanelles	Low set ears
Accessory nipples / auricles	Lymphangioma
Anal fissures	Lymphoedema
Anterior / ectopic anus	Macro / Microcephaly – familial /relative
Atypical / abnormal facies	Macroglossia
Balanced autosomal translocation	Macrognathia
Bifid tongue	Mekel's diverticulum
Bifid uvula	Meconium ileus
Birth injuries	Mental retardation
Birth marks	Metabolic disorders
Bowing tibia	Metatarsus varus
Branchial cleft / sinus	Micrognathia
Branchycephaly	Microtia / macrotia
Brushfield spots	Nasal septum deviation
Cardiomegaly	Naevus
Cephalohaematoma	Nose abnormalities – minor
Cervical rib	Ovarian cyst
Claw / club deformities	Overlapping fingers / toes
Clicky hips	Palpebral fissures
Clinodactyly	Persistent foetal circulation
Craniotabes	Persistent left superior vena
Cutis aplasia	Plagiocephaly
Cystic fibrosis	Port wine stain
Cyst – tongue	Postural deformity
Dacrostenosis	Potter's facies
Dermatoglyphic abnomalities	Preauricular sinus
Dermoid inclusion cyst	Protruding tongue
Dextraposition	Proximal thumbs
Dislocation of knee	Pyloric stenosis
Divarication of recti muscles	Ranula under tongue
Dolichocephaly	Rash
Ear abnormalities – minor	Retractile testis / testes
Extra ribs	Retrognathia
Fistula-in-ano	Sacral pits, dimples & sinuses
Flexion deformities	Scaphocephaly
Genu recurvation	Skin folds
Genetic disease – minor	Skin tags
Haemangioma	Single umbilical artery / two vessels in cord
Heart block	Splenomegaly
Heart murmurs	Spina bifida occulta
Hepatic tumour	Subcutaneous nodules
Hepatomegaly	Subluxing knee
Hernia / inguinal and umbilical	Syndactyly – webbing
High arched palate	Syphilis – intraurterine
Hooded prepuce	Talipes – postural
Hydrocoele	Toe abnormalities – minor
Hyper / Hypotelorism	Tongue tie
Hypermobile fingers	Torticollis
Hypoplastic nails	Undescended testis / testes
Laryngeal stridor	Volvulus
Laryngomalacia	Wide sutures

Hypoplastic lungs and patent ductus arteriosus were excluded if gestational age was less than 37 weeks or birth weight was less than 2,500g.

as well as the cytogenetic laboratories, histology laboratories and nursery wards in Singapore. A system of double-reporting ensured that under-ascertainment was minimised. To ensure a high quality of information provided to the registry, field visits were made by the NBDR staff for any birth defect registration with incomplete, inconsistent and uncertain information. Care was taken to ensure that requirements for the protection of personal data were fully complied. Strict measures were in place to ensure confidentiality of data and anonymisation of extracted data for analysis.

An in-house database software programme NBDR Version 1.0 for data entry and statistical analysis was developed in conjunction with the Information Service Department of KKH. Notified cases in NBDR were exported out from the registry's database. The data were anonymised to ensure strict confidentiality of data before analysis. Using MS Access 97, 7,870 cases were extracted (on April 1, 2004) meeting the following criteria: reported and notified birth defect infants between January 1, 1994 and December 31, 2000 or foetuses aborted within the same period. A total of 175 cases of miscarriage of less than or equal to 24 weeks of gestation due to chromosome disorder between January 1, 1994 and December 31, 2000 were excluded. Of these 175 excluded cases, 142 (81.1%) were 12 weeks or less, 30 (17.1%) were between 13 and 20 weeks, and three (1.7%) were between 21 and 24 weeks. MS Access 97 was used to analyse the data.

The population denominators used in computing the rates per 1,000 live births shown in the tables were obtained from the Reports on Registration of Births and Deaths from 1994 to 2000[2]. Comparisons of abortion rates along the years were evaluated by chi-square test for trend with significance at $p<0.05$. Poisson regression analysis with relevant adjustments for age and race were performed when appropriate. The exclusion list is shown in Table I. Hypoplastic lungs and patent ductus arteriosus were excluded if gestational age was less than 37 weeks or birthweight was less than 2,500g.

A foetus or baby with multiple defects was counted as one case unit, with regard to analysis of characteristics of birth defect cases. A baby or foetus can have more than one birth defect and in this registry, many of the cases had more than one birth defect. Each defect or each system defect would be counted as a unit when specific analyses for that particular defect or for that system defect

Table II. Birth defects among live births, stillbirths and abortions from 1994 to 2000.

Year	Birth defects cases			Population			Rate/1,000 live births		
	Live births & stillbirths	Abortions	Total	Live births	Stillbirths	Total	Live births & stillbirths	Abortions	Total
1994	979	161	1,140	49,554	167	49,721	19.76	3.25	23.01
1995	956	174	1,130	48,635	140	48,775	19.66	3.58	23.23
1996	907	163	1,070	48,577	150	48,727	18.67	3.36	22.03
1997	827	217	1,044	47,333	139	47,472	17.47	4.58	22.06
1998	939	222	1,161	43,664	133	43,797	21.51	5.08	26.59
1999	878	299	1,177	43,336	125	43,461	20.26	6.90	27.16
2000	792	356	1,148	46,997	143	47,140	16.85	7.57	24.43
Total	6,278	1,592	7,870	328,096	997	329,093	19.13	4.85	23.99

Table III. Ethnicity and birth defects from 1994 to 2000.

Ethnicity of mother		Overall birth defects			Live births & stillbirths			Abortions		
Race	Population live births	N	%	R	N	%	R	N	%	R
Chinese	222,560	5,333	67.8	24.0	4,096	65.2	18.4	1,237	77.7	5.6
Malay	60,886	1,617	20.5	26.6	1,483	23.6	24.4	134	8.4	2.2
Indian	26,638	627	8.0	23.5	506	8.1	19.0	121	7.6	4.5
Others	18,012	293	3.7	16.3	193	3.1	10.7	100	6.3	5.6
Total	32,8096	7,870	100	24.0	6,278	100	19.1	1,592	100	4.9

N: number of cases; %: percentage; R: rate per 1,000 live births.

Table IV. Age group and birth defects from 1994 to 2000.

Age group (in years)	Population live births	Overall birth defects			Live births and stillbirths			Abortions		
		N	%	R	N	%	R	N	%	R
<15	64	3	0.0	46.9	3	0.0	46.9	0	0.0	0.0
15-19	5,345	146	1.9	27.3	122	1.9	22.8	24	1.5	4.5
20-24	34,835	798	10.1	22.9	701	11.2	20.1	97	6.1	2.8
25-29	115,316	2,378	30.2	20.6	1,980	31.5	17.2	398	25.0	3.5
30-34	117,733	2,610	33.2	22.2	2,134	34.0	18.1	476	29.9	4.0
35-39	47,589	1,549	19.7	32.5	1,118	17.8	23.5	431	27.1	9.1
40-44	7,037	371	4.7	52.7	211	3.4	30.0	160	10.1	22.7
45-49	158	15	0.2	94.9	9	0.1	57.0	6	0.4	38.0
Unknown	19	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0
Total	328,096	7,870	100	24.0	6,278	100.	19.1	1,592	100	4.9

N: number of cases; %: percentage; R: rate per 1,000 live births.

were performed. Therefore, the defect data did not necessarily represent mutually exclusive cases. As a result, numerically adding up the number of defects would exceed the number of cases with defects.

RESULTS

Between 1994 and 2000, a total of 7,870 cases (6,278 births and 1,592 abortuses) were notified giving a rate of 23.99 (95% CI 23.47-24.52) birth defect cases

Table V. Age and chromosomal defects from 1994 to 2000.

Age group (in years)	Population live births	Overall birth defects			Live births and stillbirths			Abortions		
		N	%	R	N	%	R	N	%	R
<15	64	0	0.0	0.00	0	0.0	0.00	0	0.0	0.00
15-19	5,345	7	0.5	1.31	5	0.8	0.94	2	0.3	0.37
20-24	34,835	51	3.6	1.46	34	5.3	0.98	17	2.2	0.49
25-29	115,316	239	17.0	2.07	125	19.5	1.08	114	14.8	0.99
30-34	117,733	384	27.3	3.26	199	31.0	1.69	185	24.1	1.57
35-39	47,589	518	36.8	10.88	198	30.9	4.16	320	41.7	6.72
40-44	7,037	204	14.5	28.99	74	11.5	10.52	130	16.9	18.47
45-49	158	6	0.4	37.97	6	0.9	37.97	0	0.0	0.0
Unknown	19	0	0.0	0.00	0	0.0	0.00	0	0.0	0.0
Total	328,096	1,409	100.0	4.29	641	100.0	1.95	768	100.0	2.34

N: number of cases; %: percentage; R: rate per 1,000 live births.

Table VI. Age and non-chromosomal defects from 1994 to 2000.

Age group (in years)	Population live births	Overall birth defects			Live births and stillbirths			Abortions		
		N	%	R	N	%	R	N	%	R
<15	64	3	0.05	46.88	3	0.05	46.88	0	0.00	0.00
15-19	5,345	139	2.15	26.01	117	2.08	21.89	22	2.67	4.12
20-24	34,835	747	11.56	21.44	667	11.83	19.15	80	9.71	2.30
25-29	115,316	2,139	33.11	18.55	1,855	32.91	16.09	284	34.47	2.46
30-34	117,733	2,226	34.45	18.91	1,935	34.33	16.44	291	35.32	2.47
35-39	47,589	1,031	15.96	21.66	920	16.32	19.33	111	13.47	2.33
40-44	7,037	167	2.58	23.73	137	2.43	19.47	30	3.64	4.26
45-49	158	9	0.14	56.96	3	0.05	18.99	6	0.73	37.97
Unknown	19	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Total	328,096	6,461	100.00	19.69	5,637	100.00	17.18	824	100.00	2.51

N: number of cases; %: percentage; R: rate per 1,000 live births.

per 1,000 live births (Table II). Induced abortion constituted 71.0% (1,130 cases) while spontaneous abortion and assumed spontaneous abortion comprised 13.2% (210 cases) and 15.8% (252 cases), respectively, of the total abortions. There was a decreasing trend in birth defect incidence (19.76 to 16.85 per 1000 live births) among live births and stillbirths, and an increasing trend of abortion (3.25 to 7.57 per 1,000 live births) for birth defects (chi square for trend $p<0.0001$). The ratio of aborted to delivered birth defects increased from 1:6 in 1994 to 1:2 in 2000.

The ethnic group overall birth defect rates (per 1,000 live births) were Chinese (24.0), Malay (26.6), Indian (23.5) and Others (16.3) (Table III). With regard to live births and stillbirths, Malays appeared to have a higher rate of congenital defects at birth (24.4/1,000 live births) compared to Chinese (18.4/1,000 live births). Poisson regression analysis was performed for birth defect rates for live births and stillbirths of Malay and Chinese. After adjusting for age groups, Malays had significantly higher rate of congenital defects at birth (live births and stillbirths) compared to Chinese ($p=0.0002$).

The 25-29 years group had the lowest overall rate (22.6/1,000 live births) compared to the 19 years and below group at 32.0/1,000 live births, and the 35-39 years group at 37.4/1,000 live births, the 40-44 years

group at 62.5/1,000 live births and the 45-49 years group at 126.6/1,000 live births (Table IV). Poisson regression analysis was performed for overall birth defect rates for different age groups. After adjusting for race, there was significantly lower birth defect rate in age group 25-29 years compared to the older age groups (35-39 years group, $p<0.0001$; 40-44 years group, $p<0.001$; >45 years group, $p=0.0009$).

Table VII. Mortality ratios for birth defects (n=6,958) from 1994 to 2000.

Outcome of birth defects	N	%	R
Stillbirths	136	2.0	19.5
Early neonatal death	241	3.5	35.3
Late neonatal death	86	1.2	12.6
Post neonatal death	112	1.6	16.4
Liveborn surviving	6,383	91.7	–
Total	6,958	100.0	–
Perinatal mortality (Stillbirths and early neonatal deaths)	377	–	54.2
Neonatal mortality (early and late neonatal deaths)	327	–	47.9

N: number of cases; %: percentage; R: ratio per 1,000 births.

For stillbirths and perinatal mortality, the ratio was cases per 1,000 total births (denominator was 6,958).

For the rest, the ratio was cases per 1,000 live births (denominator was 6,822).

Chromosomal defects showed a distinct progressive increase in rate with respect to maternal age (Table V) while the rate of non-chromosomal birth defects followed a U shaped pattern with higher rates at both extremes of maternal age (Table VI). The stillbirth ratio, perinatal mortality ratio and neonatal mortality ratio for birth defects from 1994 to 2000 were 19.5 per 1000 total births, 54.2 per 1000 total births and 47.9 per 1,000 live births respectively (Table VII).

The five most common groups of anomalies (per 1,000 live births) were those of heart (9.07), musculoskeletal (4.98), chromosomal (4.35), urinary (3.12) and nervous systems (2.90) (Table VIII). The five most common aborted anomalies (per 1,000 live births) were those of chromosomal (2.40), nervous system (1.23), heart (0.95), musculoskeletal (0.85) and urinary systems (0.36). Down's syndrome was the most common chromosomal anomaly (Table IX). Common heart anomalies included ventricular septal defects and ostium secundum defects (Table X).

DISCUSSION

Birth defect registry data is vital for formulating epidemiological and management strategies that may have considerable implications for the provision of resources in the obstetric and paediatric specialties. It is also useful for etiological research either as hypotheses-generating studies, or studies directed at one specific association between a risk

Table VIII. British Paediatric Association (BPA) classification (3-digit code) of birth anomalies cases from 1994 to 2000.

		Overall		Live births & stillbirths		Abortions	
	BPA	No	Rate	No	Rate	No	Rate
Nervous system anomalies	740-742	950	2.90	545	1.66	405	1.23
Eye anomalies	743	132	0.40	132	0.40	0	0.00
Ear, face and neck anomalies	744	321	0.98	321	0.98	0	0.00
Heart anomalies	745-747	2,977	9.07	2,665	8.12	312	0.95
Respiratory system anomalies	748	246	0.75	153	0.47	93	0.28
Cleft palate and cleft lip	749	648	1.98	584	1.78	64	0.20
Gut system anomalies	750-751	564	1.72	481	1.47	83	0.25
Genital organ anomalies	752	713	2.17	693	2.11	20	0.06
Urinary system anomalies	753	1,023	3.12	906	2.76	117	0.36
Musculoskeletal anomalies	754-756	1,634	4.98	1,356	4.13	278	0.85
Integument anomalies	757	221	0.67	221	0.67	0	0.00
Chromosomal anomalies	758	1,428	4.35	642	1.96	786	2.40
Other congenital anomalies	759	274	0.84	274	0.84	0	0.00
Maternal related anomalies	760-761	12	0.04	10	0.03	2	0.01

Rate – per 1,000 live births.

Table IX. BPA classification (4-digit code) of chromosomal anomalies from 1994 to 2000.

	BPA	Overall		Live births & stillbirths		Abortions	
		No	Rate	No	Rate	No	Rate
Down's syndrome	758.0	618	1.88	336	1.02	282	0.86
Patau's syndrome	758.1	75	0.23	20	0.06	55	0.17
Edward's syndrome	758.2	219	0.67	61	0.19	158	0.48
Other autosomal anomalies	758.3	48	0.15	31	0.09	17	0.05
Balanced autosomal translocation in normal individual	758.4	24	0.07	20	0.06	4	0.01
Other conditions due to autosomal anomalies	758.5	215	0.66	70	0.21	145	0.44
Turner's syndrome/Gonadal dysgenesis	758.6	89	0.27	30	0.09	59	0.18
Klinefelter's syndrome	758.7	44	0.13	21	0.06	23	0.07
Other sex chromosome anomalies	758.8	56	0.17	27	0.08	29	0.09
Other chromosome anomalies	758.9	40	0.12	26	0.08	14	0.04

Rate – per 1,000 live births.

Table X. BPA classification (4-digit code) of heart anomalies from 1994 – 2000.

	BPA	Overall		Live births & stillbirths		Abortions	
		No	Rate	No	Rate	No	Rate
Common truncus	745.0	45	0.14	40	0.12	5	0.02
Transposition of great vessels	745.1	162	0.49	135	0.41	27	0.08
Fallot's tetralogy	745.2	189	0.58	164	0.50	25	0.08
Common ventricle	745.3	24	0.07	17	0.05	7	0.02
Ventricular septal defect	745.4	1,107	3.37	1,000	3.05	107	0.33
Ostium secundum defect	745.5	1,079	3.29	1,040	3.17	39	0.12
Endocardial cushion defect	745.6	109	0.33	66	0.20	43	0.13
Cor biloculare	745.7	2	0.01	1	0.00	1	0.00
Other specified defect of septal closure	745.8	5	0.02	4	0.01	1	0.00
Other unspecified defect of septal closure	745.9	0	0.00	0	0.00	0	0.00
Anomalies of pulmonary valve	746.0	282	0.86	256	0.78	26	0.08
Congenital tricuspid atresia and stenosis	746.1	156	0.48	137	0.42	19	0.06
Ebstein's anomaly	746.2	26	0.08	20	0.06	6	0.02
Congenital stenosis of aortic valve	746.3	27	0.08	24	0.07	3	0.01
Congenital insufficiency of aortic valve	746.4	16	0.05	13	0.04	3	0.01
Congenital mitral stenosis	746.5	21	0.06	13	0.04	8	0.02
Congenital mitral sufficiency	746.6	56	0.17	56	0.17	0	0.00
Hypoplastic left heart syndrome	746.7	98	0.30	55	0.17	43	0.13
Other specified anomalies of heart	746.8	201	0.61	158	0.48	43	0.13
Unspecified anomalies of heart	746.9	131	0.40	105	0.32	26	0.08
Patent ductus arteriosus	747.0	1,155	3.52	1,143	3.48	12	0.04
Coarctation of aorta	747.1	95	0.29	81	0.25	14	0.04
Other anomalies of aorta	747.2	115	0.35	77	0.23	38	0.12
Anomalies of pulmonary arteries	747.3	133	0.41	103	0.31	30	0.09
Anomalies of great viens	747.4	150	0.46	114	0.35	36	0.11
Absence or hypoplasia of unbilical artery	747.5	68	0.21	39	0.12	29	0.09
Other anomalies of peripheral vascular system	747.6	16	0.05	10	0.03	6	0.02
Other specified anomalies of circulatory system	747.8	46	0.14	43	0.13	3	0.01
Unspecified anomalies of circulatory system	747.9	5	0.02	4	0.01	1	0.00

Rate – per 1,000 live births.

factor and a birth defect in order to confirm or refute possible association[3,4]. To fulfil its functions optimally as a birth defect registry, common deficiencies that need to be identified and minimised are the under-notification and misclassification of major congenital malformations, under-ascertainment of additional malformations, and over-notification of trivial malformations. These have largely been addressed in Singapore's NBDR.

The national data have been enhanced by the ascertainment through multiple sources and the inclusion of all data from abortions carried out following prenatal diagnostic procedures. An exclusion list of trivial defects is also consistently maintained. Under-reporting of associated anomalies, especially in the first few years of the registry, has been addressed with the changes in database structure and new notification forms[1]. A good system of database analysis has also been implemented to ensure that additional malformations are accounted for, while avoiding duplication of cases with unique identifiers. It is also important to avoid premature analysis of cases of immediate years and the data would require at least a three-year time frame for stabilisation, as a significant number of cases are still reported after the second year.

The national data from 1994 to 2000 showed a decreasing trend in birth defects incidence (19.76 to 16.85 per 1,000 live births) among live births and stillbirths and an increasing trend of abortion (3.25 to 7.57 per 1,000 live births) for birth defects. These data were consistent with the establishment of routine antenatal ultrasound in obstetrical care in Singapore, the increasing use of prenatal diagnosis and selective termination. This study showed racial differences in the incidences of birth defects. In a this study, Malays appeared to have a higher overall rate of congenital defects as well as a lower rate of abortion compared to Chinese. This resulted in a higher rate of congenital defects at birth for Malays (24.4/1,000 live births) compared to Chinese (18.4/1,000 live births). The lower rate of abortion for birth defects was consistent with the religious and cultural background of Malays, especially relating to views on induced abortion. Late or infrequent antenatal care of Malays[5] might also be a factor for the lower rate of induced abortion for birth defects. These differences need further study.

The national data showed that both extremes of maternal age were at higher risk of non-chromosomal birth defects while advanced maternal age was at higher risk of chromosomal defects. Mothers aged 19 years and below constituted 1.96% of Singapore antenatal population from 1994 to 2000. This age group, with an incidence of overall birth defects at 32.0/1,000 live births, had a 1.4-fold higher risk of overall birth defect compared to the 25-29 years age group which had the lowest rate at 22.6/1,000 live births. Mothers aged 35 years and above constituted 16.7% of Singapore antenatal population from 1994 to 2000. With the rising proportion of advanced-age mothers in Singapore[2], this is a source of concern. The 45-49 years age group, with incidence of 126.6/1,000 live births, showed a 5.6-fold higher risk of overall birth defect when compared to the 25-29 years age group with rate of 22.6/1,000 live births. In terms of chromosomal defect risks, the 45-49 years age group (38.0/1,000 live births) showed a much higher (18.3-fold) risk than the 25-29 years age group (2.1/1,000 live births). Education of the population is necessary to ensure that mothers and the community are aware of the optimal age of motherhood in terms of birth defects risks.

In term of non-chromosomal defects, the findings of higher risks at both extremes of age were consistent with an American study which showed that advanced maternal age beyond 25 years was associated with significantly increased risks of fetuses having congenital malformations not caused by aneuploidy[6]. They were also consistent with known associations of some non-chromosomal defects, like gastroschisis with very young mothers[7]. However, the findings were different from a Canadian population-based analysis which showed no association between the incidence of birth defects of unknown aetiology and advancing maternal age[8]. These differences require further investigation.

The stillbirth ratio, perinatal mortality ratio and neonatal mortality ratio in the Singapore general antenatal population from 1994 to 2000 were 3.0/1,000 total births, 4.6/1,000 total births and 2.2/1,000 live births, respectively[2]. In contrast, the stillbirth ratio, perinatal mortality ratio and neonatal mortality ratio for birth defects in this study were much higher at 19.5/1,000 total births, 54.2/1,000 total births and 47.9/1,000 live births, respectively. These birth defects constituted 13.6% (136 of 997 total stillbirths) of population stillbirths, 25.2% (377 of 1496 total perinatal mortality cases) of population perinatal mortality, and 45.7% (327 of 716 total neonatal deaths) of population neonatal mortality between 1994 and 2000. Indeed, congenital birth defect is now a major cause of perinatal and neonatal mortality in Singapore. The mortality rates were consistent with a European study which showed the overall incidence of congenital malformations in their perinatal death-group to be

33% and lethal congenital malformations to be 70% of the cases in the neonatal death-group[9].

The most common group of anomalies were heart defects with incidence of 9.07/1,000 live births. Only a small proportion (equivalent to 0.95/1,000 live births) that were affected by heart defects were aborted, giving an incidence at birth of 8.12/1,000 live births. This was consistent with various studies where incidences varied widely from about 4/1,000 to 50/1,000 live births[10] and which showed that the heart (cardiovascular) system was usually the most common group of anomalies[11-15]. The top two most common anomalies (heart and musculoskeletal) were also the top two groups in the California and Iowa registries[15-16]. The most common aborted anomalies were those with chromosomal defects, with an abortion incidence of 2.40/1,000 live births. More than one-half (786 of 1,428 cases) of the chromosomal defects were aborted, either spontaneously or induced. This is consistent with increasingly more chromosomal defects being terminated due to increasing and better use of prenatal diagnostic techniques[1,17].

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