Mortality in Foetal Alcohol Syndrome

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Many papers about foetal alcohol syndrome (FAS) have followed the original publications,¹⁻³ and much is now known about how maternal alcohol consumption during pregnancy may affect the foetus. These effects include a wide variety of malformations,⁴ intellectual problems including mental retardation and learning disabilities⁵⁻⁷ and miscarriage and foetal death.⁸ Little has been written, however, about postnatal mortality. A literature review found only three papers in which mortality is mentioned. Spohr et al.⁹ followed 72 patients for 10 years and found that three patients (4%) had died. Two of 40 patients (5%) in a Scottish study¹⁰ had died, though all patients in this cohort were less than 12 years of age. The first 11 patients with FAS reported in the English language literature² were reviewed 10 years later by Streissguth et al.,¹¹ the oldest survivor being 14.7 years. Two of the 11 (18%) were dead.

In a cohort of 207 patients whom we have studied, 12 have died. This paper reviews these cases.

METHODS

We carried out an epidemiological study of FAS in Saskatchewan, in which we

attempted to identify all known cases of FAS in that province. We restricted our study to those with the full foetal alcohol syndrome. Details of the study have been published in this journal.¹² Briefly, each patient was born in Saskatchewan before January 1, 1993, satisfied standard diagnostic criteria for the syndrome,^{13,14} and had a history of excessive maternal alcohol ingestion in pregnancy, either by self-report of the mother or by report of reliable observers in the mother's community. Most of the patients were clients of the Alvin Buckwold Child Development Program in Saskatoon, the major referral centre for handicapped children in central and northern Saskatchewan, but cases were referred from other centres and from paediatricians, geneticists, and early childhood psychologists. Many were followed for a number of years and were seen on several occasions. We examined 192 personally at least once and reviewed the records of the other 15, each of whom had been diagnosed by paediatricians experienced in FAS. All except 13 had been born since 1972. We had direct access to records about the death of nine patients. In the others, information was given by correspondents. The cause of death as recorded on the death certificate for each case was confirmed by the Vital Statistics Division of Saskatchewan Health.

The expected number of deaths in the time period reviewed was calculated as follows. We noted the number of patient-years¹⁵ for each year from 1962 to 1992 for the age groups under 1 year, 1 to 14 years, and 15 to 30 years in our cohort. Since 86% of the cohort, and all of those who died, were North American Indians, we used the age-specific death rates for North American Indians¹⁶ to calculate the num-

ber of deaths that would be expected to occur in the patient-years in each of the three age-groups. These numbers were then summed to provide an overall expected number of deaths. In order to compare the observed deaths with the expected deaths, the observed deaths were assumed to have a Poisson distribution, the mean being equal to the expected value. A goodness of fit statistic based on the chi-square test was used for the comparison.

RESULTS

There were 12 deaths among the 207 identified cases.

Table I shows the patient-years and expected number of deaths in each of the three age groups. The overall expected number of deaths was 6.71 ($p=0.04$).

A summary of the cases and causes of death is given in Table II. The age at death ranged from 13 days to 29 years and 10 months. Seven were males. All patients were North American Indian. Congenital heart disease was the major factor in seven and a contributing factor in another. Two died from liver disease, two from systemic infection, and one from congenital abnormalities of the respiratory tract.

DISCUSSION

Our mortality rate of 5.8% is in keeping with the high rate seen in previously reported studies.⁹⁻¹¹ The actual death rate in our patients is 3.5 times what would be expected in the general population. However, the majority of our patients were North American Indians, and mortality rates for that group have been consistently higher than for the rest of the population.¹⁷ Therefore, we calculated the expected

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Table I
Calculation of Expected Number of Deaths in a Cohort of 207 Cases of FAS

Period	Patient -Years	< 1 Year		Age Group 1 - 14 Years			15 - 30 Years		
		M.R.*	Expected Deaths	Patient -Years	M.R.*	Expected Deaths	Patient -Years	M.R.*	Expected Deaths
1962-71	10	48	0.48	44	1	0.044	---	---	---
1972-81	87	32	2.78	397	0.74	0.29	18	4.5	0.08
1981-92	110	15	1.65	1353	0.74	1.00	193	2.0	0.39
TOTAL			4.91			1.33			0.47
Expected Number of Deaths = 6.71 (p=0.04)									
* Age-specific mortality rates in Saskatchewan Indians, per 1,000									

TABLE II
Information on the 12 Patients Who Died

Case	Sex	Date of Death	Age	Underlying Cause of Death	Comment
1	F	5/77	5.5ms	Tetralogy of Fallot	Waterston procedure
2	M	2/80	4yr4ms	Tetralogy of Fallot	Waterston shunt; attempted Blalock-Taussig procedure
3	M	6/80	5yr3ms	Tetralogy of Fallot	Cleft palate; Waterston procedure; attempted repair of tetralogy
4	M	9/80	1yr3ms	<i>H. Influenzae</i> meningitis	
5	M	11/83	5yr9ms	Tetralogy of Fallot	Blalock-Taussig procedure; attempted partial repair of tetralogy
6	M	3/84	1yr11ms	Bronchopneumonia, septicaemia	Ventricular and atrial septal defects; pulmonary artery banding
7	M	9/84	10yr7ms	Tetralogy of Fallot	Cleft palate; Waterston procedure; repair of tetralogy
8	M	8/86	5ms	Congenital extra-hepatic biliary atresia	Ventricular and atrial septal defects, patent ductus arteriosus
9	F	2/88	7yr6ms	Double outlet right ventricle; ventricular septal defect	Pulmonary artery banding, septal defect closure
10	F	7/89	13days	Hypoplastic left heart syndrome	Status epilepticus at 18 ms, followed by hemiplegia
11	F	9/92	29yr10ms	Congenital cirrhosis	Esophageal varices: portocaval shunts; splenectomy
12	F	4/93	2yr2ms	Tracheolaryngomalacia; laryngeal webbing	Gastro-esophageal reflux, pulmonary aspirations

number of deaths using data based on the North American Indian population.

The high mortality rate in our cohort could be an underestimate for two reasons. First, though we have been able to confirm the vital status of 185 patients in our cohort, we do not know the current status of 22. Some have left the province or been adopted, and their new addresses are not available to us. Second, some deceased FAS patients could have died before the diagnosis had been established or before referral to us or to one of our referral sources.

The deaths in this series were due primarily to the congenital anomalies caused by FAS. However, at least two of our patients died from infectious causes, and the poor growth and altered immune processes that have been reported in FAS^{8,18} may have contributed to other deaths. Our cohort was young, and the causes of death reflect this: congenital anomalies and infec-

tions are common causes of death in early childhood. It is possible that there will be further mortality in the cohort as the patients approach the age at which death from injury is all too common, and FAS patients have behavioural characteristics such as impulsiveness and poor judgement that will place them at risk.^{8,10}

Congenital malformations are common in FAS.⁸ Nine of our patients in this series had a heart defect, in seven it was the direct cause of death, and in another it was a major contributory factor. Heart malformations were present in 34 (17%) of our total cohort of 207 patients, a figure very similar to the 18% of 550 case reports of FAS compiled by Abel.⁸ The commonest cardiac lesion in our cohort was an isolated ventricular septal defect, which occurred in 10 patients, while tetralogy of Fallot was seen in 7, including 5 reported here. This is a higher incidence of tetralogy of Fallot

than the 0.9% reported in Abel's series.⁸ Two patients died from liver disease, one secondary to extrahepatic biliary atresia and the other from the effects of what was diagnosed as "congenital cirrhosis". This latter patient and two others, still alive, were previously described by us.¹⁹ One other patient died from the complications of congenital defects of the upper respiratory tract. Only one patient of the 12 did not have any congenital malformations (other than the facial abnormalities seen as part of the syndrome). Most of the patients described here had several surgical procedures, and a very complicated medical and social history. We could find no evidence that congenital malformations are commoner in American Indians than in other races,²⁰⁻²² which suggests that the high proportion of patients with congenital malformations in our cohort is a consequence of FAS, and not of racial factors alone.

The sequelae of FAS are considerable for the patients, their families, and for society. To the long list of consequences of a mother drinking excessively in pregnancy must be added the possibility of the premature death of her child.

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