Am J Hum Genet 33:470–478, 1981

An Epidemiologic Study of Congenital Malformations of the Anterior Abdominal Wall in More Than Half a Million Consecutive Live Births

PATRICIA A. BAIRD[1] AND E. C. MACDONALD[2]

SUMMARY

The records of an ongoing health surveillance registry that utilizes multiple sources of ascertainment were used to study the incidence rate of congenital malformations of the anterior abdominal wall in live-born children in British Columbia during the period 1964–1978 inclusive. No overall increase in incidence rate of these anomalies was detected during the study period. The estimated live-born incidence rates were: one in 4,175 live births for omphalocoele, one in 12,328 live births for gastroschisis, and one in 29,231 live births for prune belly. The data were analyzed with regard to sex and associated anomalies. Some practical implications regarding assessment of these infants are discussed.

INTRODUCTION

Until the last decade, most children born with major defects of the anterior abdominal wall (exomphalos or omphalocoele, and gastroschisis) did not survive. The greatly improved survival rates are attributable not only to the introduction in 1967 [1] of a method of using prosthetic material for closure of large defects, but also to improved pre- and postoperative management of these infants, particularly with respect to intravenous feeding. The increased possibility of salvaging these infants has led to a greater awareness of congenital defects of the anterior abdominal wall among pediatric surgeons and pediatricians. The purpose of this study was to review the incidence of these defects over the last 15 years in a population for which

Received August 5, 1980; revised October 15, 1980.

[1] Department of Medical Genetics, University of British Columbia, Vancouver, British Columbia, Canada.

[2] The British Columbia Health Surveillance Registry, Division of Vital Statistics, Ministry of Health, British Columbia.

good ascertainment was possible. No other study on a defined population has been published in the last 25 years. The data relate to over half a million consecutive live births during a 15-year period.

MATERIALS AND METHODS

The data in this study were derived from the records of the British Columbia Health Surveillance Registry. Only live-born cases were analyzed in detail as the ascertainment of malformations in stillborn cases is incomplete. Each affected individual may be ascertained by the Registry from a large number of different sources, the most important ones in this study being Hospital Discharge Diagnoses on infants, Physician's Notice of Birth, and Vital Registrations of Death. Discharge diagnoses from the British Columbia hospital programs are submitted to the Registry by all public hospitals in the province for children under age 7. This data source was introduced in 1966. The Physician's Notice of Birth, completed by the physician within 48 hrs of birth as required by the Division of Vital Statistics, asks if congenital malformations are present and, if so, what these are. Death registrations for children under age 1 are submitted to the Registry by the Division of Vital Statistics. These latter two sources were introduced in 1964. The study period chosen, therefore, was from 1964 to 1978 to reflect the more complete ascertainment of these defects during that time period.

To avoid duplicate entry of cases from the over 80 sources of registering, each new record is compared with an alphabetic index before inclusion in the caseload. Registry records are linked manually with provincial birth registration numbers, further reducing the likelihood of duplication. Each case reported to the Registry may have up to four different diagnoses recorded if multiple malformations exist. The organization and ascertainment methods of the Registry are described in detail by Lowry et al. [2].

The Registry uses the International Classification of Diseases (W.H.O.) (9th edition) diagnostic codes. Cases coded to those categories that might include defects of the anterior abdominal wall (756.7 and 553.1) were reviewed by a pediatrician-geneticist and sorted into the categories: omphalocoele (or exomphalos); gastroschisis; and prune belly. For the study, omphalocoele (or exomphalos) is defined as herniation of some intra-abdominal contents through the umbilical ring into the cord. This defect has a membrane over it, and may contain abdominal organs. It is thought to be associated often with additional anomalies [3]. Gastroschisis is defined as a full-thickness defect in the abdominal wall. There is no membrane over it, and it usually exposes only gut and not other abdominal organs. There is usually skin between the edge of this defect and the umbilical ring, and it is much less often associated with other anomalies than is omphalocoele [3].

Tabulations of the Registry records were made by type of defect, birth year, associated anomalies, and sex. The corresponding numbers of all live births that occurred each year in the province were provided by Statistics Canada. Frequencies for the individual birth years were examined to see if any one differed significantly from the other years, using Goodman's multiple test procedures [4].

RESULTS

There was a total of 173 cases of live-born children with a major congenital defect of the anterior abdominal wall. Table 1 shows the number of live-born cases of omphalocoele (or exomphalos) by year and sex in British Columbia. The incidence per 1,000 live births was 0.24, and the sex ratio was not significantly different from the sex ratio for provincial births. No single year differed significantly in incidence from the others. Table 2 shows the number of cases of omphalocoele plus gastrochisis in British Columbia live births for the study period (see DISCUSSION). No single

TABLE 1

CASES OF OMPHALOCOELE IN BRITISH COLUMBIA LIVE BIRTHS 1964–1978

YEAR	ALL LIVE BIRTHS	CASES			INCIDENCE/1,000 LIVE BIRTHS
		Male	Female	All	
1964	35,897	6	3	9	0.25
1965	33,669	2	2	4	0.12
1966	32,502	4	3	7	0.22
1967	32,899	3	3	6	0.18
1968	33,687	6	8	14	0.42
1969	35,383	5	5	10	0.28
1970	36,861	4	5	9	0.24
1971	34,852	4	7	11	0.32
1972	34,563	3	1	4	0.12
1973	34,352	4	3	7	0.20
1974	35,450	6	4	10	0.28
1975	36,281	3	5	8	0.22
1976	35,848	9	4	13	0.36
1977	36,691	2	5	7	0.19
1978	37,231	2	5	7	0.19
Total	526,166	63	63	126	0.24

year differed significantly from the others in incidence. The sex ratio was not significantly different from the sex ratio for provincial births.

Table 3 shows the cases of gastrochisis by year and sex. This table starts with 1969 as no cases were registered as gastrochisis in the years prior to this. There is reason to believe (see DISCUSSION) that this may be because of a lack of awareness of this entity in earlier years, with previous cases being diagnosed as omphalocoele. If the live-born incidence is calculated using the live births from 1969 on, when reporting of gastroschisis appears to have begun, it is 0.08 per 1,000 live births. If the whole

TABLE 2

CASES OF OMPHALOCOELE PLUS GASTROSCHISIS IN BRITISH COLUMBIA LIVE BIRTHS 1964–1978

YEAR	ALL LIVE BIRTHS	CASES			INCIDENCE/1,000 LIVE BIRTHS
		Male	Female	All	
1964	35,897	6	3	9	0.25
1965	33,669	2	2	4	0.12
1966	32,502	4	3	7	0.22
1967	32,899	3	3	6	0.18
1968	33,687	6	8	14	0.42
1969	35,383	6	5	11	0.31
1970	36,861	5	9	14	0.38
1971	34,852	6	9	15	0.43
1972	34,563	6	2	8	0.23
1973	34,352	7	3	10	0.29
1974	35,450	9	6	15	0.42
1975	36,281	3	5	8	0.22
1976	35,848	11	6	17	0.47
1977	36,691	3	6	9	0.24
1978	37,231	2	6	8	0.21
Total	526,166	79	76	155	0.29

TABLE 3

CASES OF GASTROSCHISIS IN BRITISH COLUMBIA LIVE BIRTHS 1964–1978

YEAR	ALL LIVE BIRTHS	CASES			INCIDENCE/1,000 LIVE BIRTHS
		Male	Female	All	
1969	35,383	1	0	1	0.03
1970	36,861	1	4	5	0.14
1971	34,852	2	2	4	0.11
1972	34,563	3	1	4	0.12
1973	34,352	3	0	3	0.09
1974	35,450	3	2	5	0.14
1975	36,281	0	0	0	...
1976	35,848	2	2	4	0.11
1977	36,691	1	1	2	0.05
1978	37,231	0	1	1	0.03
Total	357,512	16	13	29	0.08

study period is used, the incidence is 0.06 per 1,000 live births. The sex ratio of affected infants is no different from the sex ratio at birth for the province in those years, and no single year differed significantly from the others in incidence.

Cases of the prune belly syndrome are shown in table 4. The overall live-born incidence of this from 1964 to 1978 was 0.03 per 1,000 live births. There are more males than females affected, this approaching significance at the .05 level. No single year differed significantly from the others in incidence.

Table 5 shows the total number of live-born cases of omphalocoele, gastroschisis, and prune belly that had *additional* malformations recorded. The last two columns show the results if malformations thought to be a part of, or a direct consequence of, the primary diagnosis are *not* counted as "additional." The malformations omitted

TABLE 4

CASES OF PRUNE BELLY SYNDROME IN BRITISH COLUMBIA LIVE BIRTHS 1964–1978

YEAR	ALL LIVE BIRTHS	CASES			INCIDENCE/1,000 LIVE BIRTHS
		Male	Female	All	
1964	35,897	0	0	0	...
1965	33,669	0	1	1	0.03
1966	32,502	0	0	0	...
1967	32,899	2	0	2	0.06
1968	33,687	1	0	1	0.03
1969	35,383	0	0	0	...
1970	36,861	1	1	2	0.05
1971	34,852	0	0	0	...
1972	34,563	0	0	0	...
1973	34,352	1	1	2	0.06
1974	35,450	2	2	4	0.11
1975	36,281	4	0	4	0.11
1976	35,848	1	0	1	0.03
1977	36,691	0	0	0	...
1978	37,231	1	0	1	0.03
Total	526,166	13	5	18	0.03

TABLE 5

CASES OF OMPHALOCOELE, GASTROSCHISIS, AND PRUNE BELLY WITH ADDITIONAL DEFECTS

DIAGNOSTIC CATEGORY	CASES WITH ANY ADDITIONAL DEFECTS		CASES WITH ADDITIONAL "UNRELATED" DEFECTS	
	No. cases	% of total	No. cases	% of total
Omphalocoele (exomphalos)	73	58%	63	50%
Gastroschisis	14	48%	7	24%
Prune belly	16	89%	1	6%

were malrotation and intestinal atresias for omphalocoele and gastroschisis; and pulmonary hypoplasia and clubfoot for prune belly. Nine cases of prune belly syndrome had genitourinary malformations recorded.

Table 6 shows the number of cases that had additional malformations, and the particular type of additional information, when the primary diagnosis was omphalocoele.

There were 30 stillborn cases registered during the study period (27 omphalocoele, one gastroschisis, and two prune belly syndrome). The sex ratio, associated anomalies, and time distribution of the stillborn cases did not appear to differ from that of the live-born cases of omphalocoele.

DISCUSSION

Incidence

Any attempt to estimate the incidence rate of a large birth cohort will almost inevitably be based on results that do not take into account at least some of the affected individuals because, for example, of misclassification of the anomaly. However, it is believed it would be difficult to miss these malformations and that almost all would be recognized at or shortly after birth. As the Physician's Notice of Birth, Hospital Discharge Diagnoses, and Death Registrations were used as sources of ascertainment, it was felt that there would be relatively few cases of live-born children with these severe anomalies missed.

TABLE 6

NO. 126 CASES OF OMPHALOCOELE WITH SELECTED ADDITIONAL MALFORMATIONS

Additional diagnosis	No. cases
Congenital heart defect	23
Skeletal deformity	20
Genitourinary defects	18
Central nervous system malformation	9
Chromosomal trisomy	8
Diaphragm defects	7
Cleft lip and palate	7
Beckwith-Weidemann	4
Imperforate anus	3
Polydactyly	2

It is thought that between one-third and one-half of infants with omphalocoele and gastroschisis are stillborn [5, 6]. On this basis, more than the 30 stillborn cases recorded would have been expected. However, as noted, stillbirths were not analyzed in detail as malformations in stillbirths are known to be incompletely ascertained.

McKeown et al. surveyed all infants born in 1941 to 1951 in Birmingham and found one in 3,200 had omphalocoele [6]. This survey included 34 stillbirths in the 69 cases. If these are omitted, an incidence rate of one live-born case of omphalocoele per 6,501 births is obtained. This is comparable to the one case per 4,167 live births found in this study.

The incidence of gastroschisis is said to be one in 20,000–30,000 births [7]. The incidence in this study of live-born cases was one in 18,144 live births if the whole study period was considered. However, this diagnostic category did not appear to have been used prior to 1969. If the live births from that time on are used as a denominator, incidence of live-born cases of gastroschisis was one in 12,328 births. There was increased recognition of this diagnostic entity about this time, and it may be that individuals prior to then were not delineated separately from omphalocoele. For that reason, these two categories—omphalocoele and gastroschisis—were amalgamated and the time trends for them analyzed. No one year showed any significant difference in incidence when they were considered together. The incidence of these two defects together in live-born infants was one in 3,448 live births.

The incidence of the prune belly syndrome is thought to be one in 30,000–40,000 live births [8]. The incidence found in our study of live-born cases was one in 29,231 live births, which is in agreement with this estimate.

Sex

In McKeown et al.'s study [6], the male/female ratio was 1:1 for omphalocoele. Other investigators [9, 10] have noted a male preponderance. The sex ratio in Rickham et al.'s 145 cases was 3:2 [3]. We did not find this male preponderance in our study, the sexes being affected almost equally in omphalocoele. There does not appear to be any extensive information on the sex ratio of gastroschisis. In our 29 cases, there were 16 males and 13 females. This was not significantly different from the sex ratio at birth for the province. There was a marked male preponderance in our cases of prune belly syndrome with 13 of the 18 cases being male. This is in keeping with what has been found in the literature for the prune belly syndrome [11], where there is a very marked male preponderance.

Associated Anomalies

Omphalocoele. The difference between the three diagnostic groups in the frequency of associated anomalies is striking. The average incidence of associated malformations with omphalocoele in 11 large series is 67% [12]. In Rickham et al.'s series of 145 cases of omphalocoele, 37% were said to have an additional "major" anomaly. If all additional anomalies are included, 58% of our cases had an additional defect. However, this included gastrointestinal anomalies that are a consequence of omphalocoele, such as malrotations. If these are omitted, approximately

50% of our cases of omphalocoele had an additional defect not directly attributable to, or part of, the omphalocoele. This marked association with additional anomalies is the main reason for the poorer prognosis of cases of omphalocoele compared to cases of gastroschisis.

In McKeown et al.'s series [6], 20% of cases of omphalocoele had anencephaly. Four of our 126 live-born cases had anencephaly or a neural tube closure defect. Rickham et al. found a frequent association of cardiovascular malformations with omphalocoele, with 43 of his 143 cases having a cardiovascular anomaly. This is in keeping with other series in the literature. Twenty-three of our 126 cases had a congenital heart defect.

Eight of our cases of omphalocoele had a chromosomal trisomy diagnosed. If the cases of omphalocoele with cleft lip and palate [8] and polydactyly [3] are included as considered likely to represent cases of trisomy 13, then 13% of our cases of omphalocoele had a trisomy syndrome. This has the practical implication that chromosomes should be examined in all cases of omphalocoele to give an accurate diagnosis so that appropriate recurrence risk figures can be used in counseling the parents. We found that the Beckwith-Weidemann syndrome had been diagnosed in four of our 126 cases. Rickham et al. found 17 of his 143 cases also had this diagnosis. More than 50% of infants with Beckwith-Weidemann syndrome have hypoglycemia in the neonatal period, and anticipation of this complication can prevent central nervous system damage. It is therefore recommended that all infants with omphalocoele have their blood sugars carefully monitored.

Gastroschisis. There has been controversy on whether gastroschisis and omphalocoele have a common embryogenesis. Collins and Schumacher put forward the thesis that gastroschisis is the end result of intrauterine rupture of an exomphalic sac with absorption of fragments of the sac and growth of skin between the edge of the defect and insertion of the cord [13]. However, most authorities feel that these two entities are clinically different [14], and certainly the proportion of cases in the two groups that have associated anomalies is markedly different. Patients with gastroschisis have a low incidence of associated anomalies when compared with infants with omphalocoele [15]. This was true in our series in which less than a quarter of gastroschisis cases had anomalies not directly related to gastroschisis. The additional defects seen in our series were largely those to be expected from the embryology of the defect, namely, congenital heart defects (four cases) and diaphragm and sternal defects (two cases).

Prune Belly. Sixteen of the 18 infants with prune belly syndrome had additional anomalies. As expected from the pathogenesis of this syndrome, half of the infants had a genitourinary obstructive malformation identified. It was of interest that almost all of the other malformations associated with this category were explicable on the basis of oligohydramnios from a urinary tract obstruction. The malformations were clubfeet (five cases) and pulmonary hypoplasia (three cases).

The proportion of each of the three diagnostic categories with additional diagnoses did not appear to change significantly over the years of the study period.

Clinical Implications. The recurrence risk for these three malformations is relatively low overall [16]. However, in each of the categories there are several cases of

more than one individual affected in a sibship [3, 6, 17]. In our study, none of the cases were known to have an affected relative. Ultrasound scanning of future pregnancies may be of help in detecting these anomalies. Amniocentesis looking for an elevated alpha fetoprotein in gastroschisis and omphalocoele [18] may be of help to further investigate cases in which the ultrasound investigation is equivocal, or for parents who are extremely anxious about recurrence. Brock [19] suggested that theoretically the level of alpha fetoprotein would be low in cases in which the fetus is not excreting urine into the amniotic fluid. However, there are several documented cases of renal agenesis or bladder neck obstruction [18, 20, 21] in which elevated levels of alpha fetoprotein have been measured. Therefore, the level of alpha fetoprotein in amniotic fluid cannot be used at present as a reliable indicator for these types of urinary tract malformations.

Accurate diagnosis is essential to appropriate counseling in these cases. It is suggested that a karyotype be analyzed on all cases of omphalocoele and the blood sugars be carefully monitored because of the association of chromosome anomalies and the Beckwith-Weidemann syndrome with this defect.

ACKNOWLEDGMENTS

We wish to acknowledge the help of Mr. S. H. Uh in statistical analysis. Strict conditions of confidentiality are maintained with respect to the files of the Health Surveillance Registry.

REFERENCES

1. Schuster SR: A new method for the staged repair of large omphalocoeles. *Surg Gynecol Obstet* 125:837–850, 1967
2. Lowry RB, Miller JR, Scott AG, Renwick DHG: The British Columbia Registry for Handicapped Children and Adults: evolutionary changes for 20 years. *Can J Public Health* 66:322–326, 1975
3. Rickham PP, Lister J, Irving IM: *Neonatal Surgery*, 2nd ed. Toronto, Butterworth, 1978
4. Goodman LA: The analysis of multidimensional contingency tables: stepwise procedures and direct estimation methods for building models for multiple classification. *Technometrics* 13:33–61, 1971
5. Rickham PP, Lister J, Irving IM: *Neonatal Surgery*, 2nd ed. (McAllister: personal communication quoted), Toronto, Butterworth, 1978, p 313
6. McKeown T, McMahon BK, Record BG: An investigation of 69 cases of exomphalos. *Am J Hum Genet* 5:168–175, 1953
7. Rickett LK: Gastroschisis, in *Birth Defects Compendium*, 2nd ed, edited by Bergsma D, The National Foundation–March of Dimes, New York, Alan R. Liss, 1979
8. Nelson WE, ed.: *Pediatrics Textbook*, 11th ed. Philadelphia, London, Toronto, W.B. Saunders, 1979, p 1569
9. Bay Nielson H, Larsen E: Omphalocoele. *Dan Med Bull* 10:75–79, 1963
10. O'Leary CM, Clymer LE: Umbilical hernia. *Am J Surg* 52:38–43, 1941
11. Ives EJ: The abdominal deficiency triad syndrome—experience with ten cases. *Birth Defects: Orig Art Ser* 10:127–135, 1974
12. Hutchin P: Gastroschisis with antenatal evisceration of the entire gastro-intestinal tract. *Surgery* 57:297–301, 1965
13. Collins DL, Schumacher AE: Omphalocoele ruptured before birth, in *Proceedings Paediatric Surgical Congress*, Melbourne, Australia, Melbourne Royal Children's Hospital, 1970, p 21
14. Moore TC: Gastroschisis and omphalocoele: clinical differences. *Surgery* 82:561–568, 1977

15. Moore TC, Stokes GE: Gastroschisis. *Surgery* 33:112–120, 1953
16. Czeizel A: Recurrence risk of omphalocoele (Letter to the editor). *Lancet* II:470, 1979
17. Paucqt H, Gellé P: Hernia ombikicale embryonnaire récidivante chez trois foetuses succesifs. *Bull Soc Obstet Gynecol Paris* 25:296–297, 1936
18. Vinson PC, Goldenberg RL, Davis RO, et al.: Fetal bladder-neck obstruction and elevated amniotic fluid fetoprotein (Letter to the editor). *N Engl J Med* 297:1351, 1977
19. Brock DJH: Mechanisms by which amniotic fluid alpha fetoprotein may be increased in fetal abnormalities. *Lancet* II:345–346, 1976
20. Seller MJ, Berry AC: Amniotic fluid alpha-fetoprotein and fetal renal agenesis (Letter to the editor). *Lancet* I:660, 1978
21. Balfour RP, Lawrence KM: Raised serum AFP levels and fetal renal agenesis (Letter to the editor). *Lancet* I:317, 1980