Fetal, perinatal, and infant death with congenital renal anomaly

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Aims: To ascertain why 19.6% of pregnancies in which a fetal renal anomaly has been detected fail to produce a surviving child, and whether antenatal diagnostic accuracy has altered since specialised fetal medicine units were established in 1995.

Methods: An analysis of deaths was conducted among fetuses and babies with a congenital abnormality in the urinary tract notified to the Northern Region Congenital Abnormality Survey (NorCAS). There were 560 deaths among 2857 cases with an anomaly in the urinary tract delivered between 19 February 1984 and 21 March 2000.

Results: Renal anomaly was the cause of death in 323 (57.7%) cases. Excluding 10 which were not screened, 126 (60%) of 210 pre-1995 had been suspected antenatally and 81 (78.6%) of 103 post-1995. No abnormality had been suspected in 39 (18.6%) cases pre-1995 and four (3.9%) post-1995. Postnatal death occurred in 89 (41.4%) pre-1995 and in 13 (12%) post-1995. There were 209 cases of death caused by anomalies in other systems but with a renal anomaly present, of which 66 (31.6%) were chromosomal and 36 (54.5%) had a horseshoe kidney. Of the cases with a horseshoe kidney, 56.3% had a chromosomal anomaly.

Conclusions: The antenatal diagnosis of renal anomalies which cause death did not improve significantly in the second period of this study. However, the number of false positive antenatal diagnoses and the number of postnatal deaths were significantly lower and the number of pregnancy terminations were significantly higher. This reduced the risk of delivering a live baby with an unexpected fatal renal anomaly.

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An analysis of Northern Congenital Abnormality Survey (NorCAS) data showed that 19.6% of pregnancies in which a congenital anomaly in the fetal urinary tract had been identified failed to produce a living child. In view of the number of minor renal anomalies recognised, such as moderate renal pelvic dilatation, this seems a high mortality. The causes are examined with particular emphasis on the accuracy of antenatal diagnosis, and whether this has changed since the introduction of specialised fetal medicine units in 1995. This is the most important factor in the effective and sympathetic management of a pregnancy in which the fetus has a life threatening developmental anomaly.

METHODS

NorCAS was initiated in 1984. It covers all hospitals in the Northern Region of England (excluding South Cumbria since the end of 1993). The population of this area is approximately 3 million with a mean annual birth rate of 39 000. All antenatally suspected and/or postnatally diagnosed congenital anomalies in all systems at all gestational ages up to the postnatal age of approximately 1 year are included. A full description of all aspects of the survey has been published previously.¹ A total of 14 487 cases delivered between 19 February 1984 and 21 March 2000 were notified to the survey, including 2880 (19.9%) with an anomaly in the urinary tract. Analyses of these have been published elsewhere.²⁻⁵ Cases in which antenatal or postnatal death had occurred for any reason were entered into a separate non-attributable database. Postmortem examination reports were carefully scrutinised for relevant naked eye and microscopic information.

RESULTS

Table 1 shows the number of deaths, pregnancy terminations, and postmortem examinations performed in cases with a urinary anomaly, compared with all cases notified to NorCAS

Table 1 Number (%) of deaths, pregnancy terminations, and postmortem examinations performed in cases with a urinary anomaly, compared with all cases notified to NorCAS during the same time period

	All cases	Renal cases
Total notified	14487	2857*
Deaths	4467 (30.8)	560 (19.6)
Terminations	1960 (13.5)	290 (51.8)
Postmortem examinations	2116 (14.6)	517 (92.3)

*Total notified 2880; unknown pregnancy outcome in 23.

during the same time period. Of the total, 323 deaths were due solely to the renal anomaly, 209 died with a renal anomaly but not because of it, and in 28 no anomaly of any kind was found after death. Figure 1 shows these data graphically.

Death because of renal anomaly (323 cases)

Table 2 shows the antenatal diagnostic sensitivity and predictive values in these cases, excluding 10 in whom no antenatal screening examination was performed. The patients are separated into those born before or after 1 January 1995.

Bilateral renal agenesis (80 cases) and *polycystic renal disease* (78 cases) were the commonest anomalies; 105 died antenatally, of which 91 were a result of pregnancy termination, and the remainder caused by intrauterine death, stillbirth, or abortion. Postnatal death (53 cases) was almost entirely a result of pulmonary hypoplasia and occurred within the first week of life.

Bladder outlet obstruction (72 cases) was another major cause. Of these, 44 (61.1%) were correctly suspected; 56 died antenatally, 42 because of pregnancy termination. The majority of postnatal deaths occurred within a week of birth and were caused by pulmonary hypoplasia.

Figure 1 Outcome distribution.

Other diagnoses of note were 30 cases of *bilateral renal dysplasia/hypoplasia* of which 11 (36.7%) were terminated, and 12 cases of *multicystic kidney*, 10 of which had contralateral renal agenesis and one a horseshoe kidney; in one case which was terminated, no abnormality was found postnatally (see below). Table 3 shows the proportion of screened cases of three of the major renal anomalies which were correctly suspected antenatally and the odds ratios (OR) comparing periods before and after the beginning of 1995. Also included is a

comparison of the number of pregnancy terminations and postnatal deaths between the two time periods. For comparison with table 2, table 4 shows a similar analysis of crude data of survivors of congenital renal anomaly.

Unsuspected diagnoses

Of the deaths caused by renal anomalies, no abnormality of any kind had been suspected antenatally in 39 cases before 1995. Among the postnatal diagnoses in this group were bilateral renal agenesis, polycystic renal disease, and congenital urethral obstruction. All but seven died postnatally from pulmonary hypoplasia or renal failure. There were only four unsuspected cases after the beginning of 1995: all had major renal anomalies and died antenatally.

False positive diagnoses

There were 20 (9.5%) cases before 1995 and eight (7.8%) after 1995. This difference is not significant (OR 0.82, 95% CI 0.35 to 4.91). Postmortem examination was performed in all and the urinary tract found to be normal. Death was a result of termination of pregnancy in 10 cases (five of these possibly avoidable); to intrauterine death, stillbirth, and abortion in 12; and to postnatal causes (pulmonary, sudden infant death, non-accidental injury, brain anomaly) in the remainder. The predominant antenatal diagnosis was bilateral renal agenesis (13 cases), followed by polycystic renal disease (four cases), and bladder outflow obstruction (two cases). Renal pelvic dilatation was suspected in seven cases: three of these died antenatally; death in the remainder was not anomaly related.

Possible avoidable death

Avoidable death (death not from natural causes but from action or inaction by clinicians) occurred in 10 (4.8%) cases before 1995 and six (5.8%) after 1995. This difference is not

Table 2 Death due to renal anomaly alone (excludes 10 cases with no antenatal screening examination)

	Anomaly suspected		
	Yes	No	Total
<i>Birth date before 1 January 1995</i>			
Anomaly confirmed			
Yes	126	84	210
No	20	0	20
Total	146	84	230
Sensitivity	0.86		
Positive predictive value	0.6		
<i>Birth date on or after 1 January 1995</i>			
Anomaly confirmed			
Yes	81	22	103
No	8	0	8
Total	89	22	111
Sensitivity	0.91		
Positive predictive value	0.79		
Odds ratio correctly diagnosed	0.75		
95% CI	0.52 to 1.08		

Table 3 Number (%) of deaths due to renal anomaly; antenatal diagnosis in screened pregnancies

Diagnosis	Before 1 January 1995			On or after 1 January 1995		
	Number	Antenatal diagnosis		Number	Antenatal diagnosis	
All cases	210	Correct	126 (60)	103	Correct	81 (78.6)*
Bilateral renal agenesis	55	Correct	35 (63.6)	22	Correct	19 (86.4)†
Polycystic renal disease	57	Correct	38 (66.7)	18	Correct	17 (94.4)‡
Bladder outlet obstruction	40	Correct	18 (45)	28	Correct	20 (71.4)§
Pregnancy terminations			99 (47.1)			82 (79.6)¶
Postnatal deaths			89 (42.4)			13 (12.6)*

*Odds ratio 0.76 (95% confidence intervals 0.53 to 1.1).

†Odds ratio 0.74 (95% confidence intervals 0.35 to 1.55).

‡Odds ratio 0.71 (95% confidence intervals 0.32 to 1.54).

§Odds ratio 0.63 (95% confidence intervals 0.28 to 1.4).

¶Odds ratio 1.69 (95% confidence intervals 1.16 to 2.46).

**Odds ratio 3.36 (95% confidence intervals 1.79 to 6.29).

Table 4 Survivors of renal anomalies (excludes two cases with no antenatal screening examination)

	Anomaly suspected		
	Yes	No	Total
<i>Birth date before 1 January 1995</i>			
Anomaly confirmed			
Yes	581	151	732
No	877	0	877
Total	1458	151	1609
Sensitivity	0.4		
Positive predictive value	0.79		
<i>Birth date on or after 1 January 1995</i>			
Anomaly confirmed			
Yes	395	41	436
No	250	0	250
Total	645	41	686
Sensitivity	0.6		
Positive predictive value	0.91		
Odds ratio correctly diagnosed	1.56		
95% CI	1.36 to 1.86		

significant (OR 0.82, 95% CI 0.29 to 2.31). One of these was a male baby who died at 8.5 months from an acute urinary tract infection and septicaemia. He had unsuspected posterior urethral valves and unilateral renal agenesis. Pregnancy was terminated in the remainder, including four suspected cases of bilateral renal agenesis, one of polycystic renal disease, and one with a renal cyst; all of these had normal kidneys at post-mortem examination. Pregnancy in three cases of suspected bladder neck obstruction/posterior urethral valves was terminated at 13–14 weeks gestation; at postmortem examination all had histologically normal kidneys. Pregnancy in two further cases had to be terminated at 14 weeks, in one because

of uterine infection following fetal bladder aspiration, and in another because of a failed vesicoamniotic shunt. Other suspected diagnoses included one with vesical agenesis and two with multicystic kidney and contralateral renal agenesis/dysplasia; at postmortem examination the bladder and kidneys in these cases were normal. Pregnancy was terminated in one case with suspected bilateral pelviureteric junction obstruction; at postmortem examination the condition was surgically operable.

Death with a urinary anomaly but caused by anomalies in other systems

Death occurred in 209 cases in which a renal anomaly was present but in which death was caused by anomalies in other systems. Postmortem examination was performed in 197 (94.3%). Pregnancy had been terminated in 97 (46.4%). In eight cases no antenatal screening examination was performed; two of these pregnancies were terminated for obstetric complications, the others suffered intrauterine death or abortion. Of 134 screened cases before 1995, no abnormality was suspected antenatally in 34; of 67 after 1995, no abnormality was suspected in eight: this difference is not significant (OR 0.47, 95% CI 0.21 to 1.07). Table 5 shows the anomalies which proved fatal and the urinary anomalies which accompanied them. The commonest of the fatal anomalies were chromosomal defects, and the commonest urinary tract anomaly was horseshoe kidney. Of the chromosomal anomalies, the commonest was trisomy 18 (29 cases) followed by Turner's syndrome (13 cases), trisomy 21 (four cases), trisomy 13 (three cases), and miscellaneous others (17 cases). There were 64 cases in the whole series which had a horseshoe kidney; 36 (56.3%) of these had a chromosomal anomaly, trisomy 18 being the commonest (17 cases), followed by Turner's syndrome (12 cases), and other miscellaneous types (seven cases). Of 85 cases in the whole series which had a chromosomal anomaly, 36 (42.4%) had a horseshoe kidney.

Table 5 Death due to anomalies in other systems

Fatal anomalies		Renal anomalies	
Chromosomal	66	Horseshoe kidney	64
Multiple system	29	Unilateral renal agenesis	42
Neural tube	23	Multicystic kidney	20
Cardiac	14	Ectopic kidney	17
Brain	14	Unilateral renal dysplasia	12
Miscellaneous others	63	Pelviureteric junction obstruction	11
		Megaureter	7
		Miscellaneous others	36

DISCUSSION

There are few, if any, fetal anomaly surveys of the duration, size, and scope of NorCAS, so it is not possible to make comparisons with experience from other centres. EUROCAT,⁶ for example, does not register cases delivered before 20 weeks gestation and includes only renal agenesis and cystic disease for urinary tract anomalies. Isaksen and colleagues⁷ analysed the postmortem examination findings in 112 fetuses with urinary system anomalies. In their series, 45% of the pregnancies were terminated; in four cases major renal anomalies were not suspected antenatally, and in a further four the renal anomaly was missed, even though anomalies in other systems were ascertained. No mention was made of coexistent chromosomal anomalies.

This study has the advantages of large numbers and a high postmortem examination rate, so that diagnoses are reliable. Postmortem examination was performed in 274 of 290 (94.5%) pregnancies which were terminated. It is clear that the majority of renal anomalies which are the primary cause of fetal, perinatal, and infant death are untreatable; those who survived pregnancy died in the first few days of life from pulmonary hypoplasia and/or renal failure. It is unusual for attempts to be made to save such newborns by dialysis and ventilation. Thus it is important to know, from the experience of a large series of cases, what proportion of the anomalies can be predicted accurately antenatally and the likely outcome of such pregnancies. Using these data parents can be given reliable information about the diagnosis and prognosis for a fetus found to have a major renal anomaly and decide whether they wish to continue with the pregnancy.

Although table 3 shows that there appears to have been an improvement in the accuracy of antenatal diagnosis of major renal anomalies since the inception of specialised fetal medicine units at the beginning of 1995, in no group does the pre- and post-1995 difference reach statistical significance. Neither does the number of false positive diagnoses. However, significantly more pregnancies were terminated and significantly fewer deaths occurred postnatally after the beginning of 1995. Thus, there has been a reduction in the number of pregnancies in which the fetus has an unsuspected fatal renal anomaly and is born alive, with consequent family distress. In contrast to the apparent absence of an improvement in the accuracy of antenatal diagnosis in cases which did not survive, table 4 suggests that this did occur in survivors. One possible reason for this is that, after the beginning of 1995, there was more effective postnatal investigation of suspected antenatal renal pelvic dilatation. Before 1995, a structural abnormality in the urinary tract was found in 267 of 1264 cases which had antenatal renal pelvic dilatation; after the beginning of 1995 the equivalent figures were 141 of 484 (OR 1.38, 95% CI 1.1 to 1.74).

The number of avoidable deaths was small and the difference between the two time periods was not significant. Interventional obstetrics played a part in two cases in the post-1995 period. In the early phase errors were caused by misinterpretation of ultrasound findings, while in the later phase they were caused by a decision to terminate pregnancy, perhaps taken at too early a stage.

It is noteworthy that among the deaths in which a renal anomaly was present, but was not the cause of death, were many with chromosomal anomalies. The majority were trisomy 18 (29 cases), followed by 17 with mixed anomalies and 13 with Turner's syndrome. The high postmortem examination rate in the study revealed a large number of horseshoe kidneys. In 36 of these (56.3%) there was also a chromosomal anomaly, mostly Turner's syndrome and trisomy 18. Thus if a horseshoe kidney is suspected antenatally, it would be wise to search for other signs of a chromosomal anomaly.

This study has shown that, when viewed against the large number of renal anomalies which are suspected antenatally, the proportion that cause pre- or post-natal death is high. There appears to have been an increase in the number correctly diagnosed antenatally since the introduction of specialised fetal medicine units in 1995, but the change is not statistically significant. However, the number of terminations has risen and the number of postnatal deaths fallen significantly so that the risk of a baby being born with an unexpected and fatal renal anomaly has been reduced.

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