Urological anomalies in the Northern Region Fetal Abnormality Survey

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Abstract

From 1 January 1985 to 31 December 1990, the Northern Region Fetal Abnormality Survey received 736 notifications of fetuses with suspected urological abnormalities; a prevalence of three per 1000 births. There was a male:female ratio of 2:1, the ratio was higher in obstructive than in intrinsic renal parenchymal lesions. Overall diagnostic sensitivity was 68.9% and positive predictive value 50.8%. Hydronephrosis was the most frequent antenatal diagnosis (421 cases, 57.2%); 233 (55.3%) of these were found to be normal postnatally. There were 52 other false positive diagnoses. Of 113 babies with confirmed hydronephrosis antenatal diagnosis was correct in 97, sensitivity 85.8%, specificity 48.1%; 1.8% of these had chromosome defects. In 33 cases of bilateral renal agenesis antenatal diagnosis was correct or potentially correct in 24, sensitivity 72.7%, specificity 98.9%. Only six of 26 babies with posterior urethral valves were suspected, sensitivity 23%, specificity 98.7%. Mortality rate in 91 babies with unsuspected abnormalities was 39.6%; overall mortality was 24.2%. Unsuspected abnormalities occurred more frequently when mothers were not scanned after the 16th week of pregnancy.

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The detection of developmental abnormalities in the fetus is regarded now as an essential component of antenatal screening. Among the most frequently suspected and, historically, the earliest recognised¹ are those affecting the urinary tract. Because of this it is important to evaluate the true reliability of antenatal diagnosis: information in the literature mostly describes relatively small series of cases seen in hospital departments.²⁻⁵ The Northern Region Fetal Abnormality Survey registers data from a population of 3.1 million from which it is possible to derive accurate correlations of antenatal with postnatal diagnoses and to record the number and nature of unsuspected diagnoses.

The purpose of this paper is to analyse the fetal urinary tract abnormalities notified to the survey between 1 January 1985 and 31 December 1990 so as to identify the sensitivity, specificity, and predictive value of the antenatal diagnosis of these abnormalities in the Northern region.

Patients and methods

The Northern Region Fetal Abnormality Survey was started on 1 January 1985 after a successful pilot scheme run during the previous year. The methods used to organise the survey and the sources of the information enlisted have previously been described.⁶⁻⁸

Results

NOTIFICATIONS

Table 1 shows the number of urological cases notified by year, the annual number of registered births in the Northern region, and the number of notifications per 1000 births. Although birth rate remained constant, the rate at which notifications were made increased by 225% during the six year period: in the final year, however, there were only nine more notifications.

GENERAL ANALYSIS

A general analysis of the data is shown in tables 2A and B. In the cases suspected antenatally and confirmed the urinary tract abnormality suspected antenatally was not necessarily identically same as the urinary tract abnormality found postnatally. For example, a baby with a multicystic kidney might have been suspected antenatally to have a hydronephrosis.

SEX INCIDENCE

There were 483 (65.6%) males and 242 (33.9%) females, a ratio of 2:1; in 11 (1.5%) the sex of the product of conception was not specified. The sex ratio remained constant throughout the time period. To determine whether the sex difference was biased towards a particular type of abnormality the cases were divided into two groups: those with hydronephrosis and those with renal cystic disease, dysplasia, or agenesis (table 3). The

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Table 1 Number of registered births and notifications by year in the Northern region

	1985	1986	1987	1988	1989	1990	Total	Mean
Births	41 101	40 462	40 603	40 324	39 297	40 841	242 628	40 438
Notifications	56	82	100	143	173	182	736	122.7
Notifications/1000 births	1.4	2.0	2.5	3.5	4.4	4.5	3.0	3.0

Table 2 Analysis of the data

<i>(A) General analysis</i>			
No of cases suspected antenatally and confirmed			292
No of cases suspected antenatally and not confirmed			285
No of cases with no suspected abnormality			91
Non-urinary abnormalities suspected			41
Postnatal diagnosis unknown			13*
No antenatal scan			8
Non-urinary abnormalities found postnatally			6
Total			736
<i>(B) Tabular general analysis</i>			
	Urological abnormality:		
Scan result:	Present	Absent	Total
Positive	292	291	583
Negative	132	X	X
Total	424	X	X
	Sensitivity 68.9%		
	Positive predictive value 50.1%		

X = see text.

*Includes one with polycystic disease.

Table 3 Sex incidence by diagnosis

Sex	Diagnosis		
	Obstructive	Parenchymal	Total
Male	89	103	192
Female	37	72	109
Total	126	175	301

 χ^2 p = 0.032.

Odds ratio M:F = 1.7:1.

Table 4 Postnatal diagnosis in babies suspected antenatally to have renal dilation: hydronephrosis

	Antenatal diagnosis			
	Unspecified	Unilateral	Bilateral	Total
Total No cases	38	230	153	421
No with hydronephrosis diagnosed postnatally:				
Unspecified	3	0	3	6
Unilateral	2	51	16	69
Bilateral	2	2	18	22
Total	7	53	37	97

ratio for the hydronephrosis group was 2.4:1 and for the second group 1.4:1.

UPPER URINARY TRACT DILATATION SUSPECTED ANTENATALLY

This is the commonest finding in the fetal urinary tract during antenatal scanning: it was suspected unilaterally in 230 fetuses and bilaterally in 153; laterality was not specified in 38. These represent 57.2% of all notified cases.

Table 5 Postnatal diagnosis in babies suspected antenatally to have renal dilatation: other abnormalities

	Antenatal diagnosis			
	Unspecified	Unilateral	Bilateral	Total
No of infants normal postnatally	21	124	88	233
No with other abnormalities diagnosed postnatally:				
Ureteric reflux	3	7	6	16
Multicystic kidney	0	14	1	15
Duplex kidney	2	10	3	15
Megaureter	1	6	3	10
Unilateral renal dysplasia	0	5	1	6
Urethral valves	0	2	4	6
Others	1	4	3	8
Total	7	48	21	76
Unknown	3	3	6	12
Non-urinary	0	2	1	3

Table 6 Number of babies with postnatally confirmed hydronephrosis by diagnosis

Antenatal diagnosis	No of babies
Hydronephrosis	97
Nil suspected	5
Multicystic kidney	3
Not scanned antenatally	2
Polycystic kidney	2
Unilateral renal dysplasia	1
Bladder neck obstruction	1
Sacral teratoma	1*
Spina bifida	1*
Total	113

*Both had multiple system defects including urinary.

Table 4 shows the number in which significant renal pelvic hydronephrosis (putative pelviureteric junction obstruction) was found postnatally and table 5 the number in which other postnatal diagnoses transpired. In 12 babies the postnatal diagnosis was unknown; one of these was an antepartum stillbirth at 36 weeks' gestation in which no necropsy was performed and the other 11 were discharged from hospital without a postnatal ultrasound examination and were lost to follow up. Table 6 shows the antenatal diagnosis in 113 babies with postnatally confirmed hydronephrosis and table 7 tabulates the scan results in the cases with urinary tract dilatation.

CHROMOSOME DEFECTS

Four (1%) of the babies whose kidneys were thought antenatally to be dilated were found to have chromosome defects: two had trisomy 13 and one trisomy 18; all of these died. The fourth baby had a de novo unbalanced translocation, 46,XX,-9,-18,t(9q18p),+1(9p) and survived. In two of the babies the dilatation was not confirmed postnatally: thus in babies with confirmed hydronephrosis the incidence of chromosome defects was 1.8%.

FALSE POSITIVE DIAGNOSES

Some false positive diagnoses are of critical importance because they may influence decisions concerning the management of pregnancy. Two hundred and thirty three (55.3%) babies suspected antenatally to have upper urinary tract dilatation were found on postnatal examination to be normal. Two factors that might have influenced this finding were examined, namely year of birth and gestational age at the time the dilatation was first suspected. The proportion of normal babies was similar in every year except 1989 when there were 72.6%. When dilatation was first suspected in the later stages of pregnancy there was a tendency for the number of normal babies to rise. This may be due to the

Table 7 Hydronephrosis and scan results

Scan result	Hydronephrosis		
	Present	Absent	Total
Positive	97	324	421
Negative	16	299	315
Total	113	623	736

Sensitivity 85.5%, specificity 48%, positive predictive value 23%, negative predictive value 94.9%, and prevalence 0.15.

Table 8 Number of normal babies suspected antenatally to have abnormal kidneys by diagnosis

Antenatal diagnosis	No of babies
Bilateral renal agenesis	8
Polycystic kidney	7
Multicystic kidney	7
Unilateral renal dysplasia	5
Renal cyst	6
Urethral valve	4
Unilateral renal agenesis	4
Bilateral renal dysplasia	3
Ascites	3
Megaureter	2
Duplex kidney	2
Bladder neck obstruction	1
Total	52

high urine output that is known to occur in the term mature fetus.⁹⁻¹¹ Other false positive diagnoses are shown in table 8.

NON-URINARY ABNORMALITIES FOUND POSTNATALLY

There were six babies in whom urinary anomalies were incorrectly suspected antenatally but who were found postnatally to have defects in other systems. One baby in whom urethral valves were suspected was a girl with hydrocolpos. Another baby thought to have a multicystic kidney had congenital lung cysts and yet another diagnosed as having unilateral renal agenesis had cystic hygroma. Three babies in whom renal dilatation was suspected had respectively, exomphalos, a branchial cleft, and a cardiac defect.

FALSE NEGATIVE DIAGNOSES

Table 9 lists the unsuspected diagnoses.

Eight mothers were not scanned antenatally; table 10 lists the diagnoses which were missed for this reason.

Table 9 Number of babies with unsuspected urological abnormalities by diagnosis

Diagnosis	No of babies
Ureteric reflux	12
Unilateral renal dysplasia	12
Unilateral renal agenesis	11
Urethral valve	9
Bilateral renal agenesis	7
Polycystic kidney	6
Hydronephrosis	5
Ectopia vesicae	5
Bilateral renal dysplasia	4
Multicystic kidney	4
Epispadias	3
Duplex kidney	2
Megaureter	2
Urethral atresia	2
Ectopia cloacae	2
Absent bladder	1
Bladder neck obstruction	1
Bladder rupture	1
Urethral diverticulum	1
Prune belly	1
Total	91

Table 10 Number of babies whose mothers were not scanned during pregnancy: by diagnosis

Diagnosis	No of babies
Hydronephrosis	2
Duplex kidney	1
Bilateral renal agenesis	1
Unilateral renal agenesis	1
Polycystic kidney	1
Urethral valve	1
Ureteric reflux	1
Total	8

NON-URINARY ABNORMALITIES SUSPECTED ANTENATALLY

Forty one babies whose urinary tract abnormalities were not suspected antenatally were notified because they were thought to have abnormalities in other systems. However, in many cases the antenatal diagnosis was correct and the urological abnormality was coincidental. In others the suspected diagnosis was nearly correct: for example, four babies were thought antenatally to have abdominal wall defects; postnatally, two had ectopia vesicae, one had a prune belly, and one had urethral valves with an abdominal wall defect. Four babies with chromosome defects were diagnosed antenatally; in three the diagnosis was correct and in the fourth the baby had multisystem anomalies. Neural tube or cerebral abnormalities were suspected in 15 babies. These were confirmed in all but one and this fetus was thought to be anencephalic and the pregnancy was terminated; there was no neural tube defect but there was bilateral renal dysplasia. An antenatal diagnosis of cystic hygroma was made in five cases; two of these aborted and the remainder were terminated. The antenatal diagnosis was confirmed in all these babies; in addition, four had horseshoe kidneys and one an epispadias. Of three cases thought antenatally to have intestinal atresia two actually had unilateral renal dysplasia and one a duplex kidney: all these babies required nephrectomy.

GESTATIONAL AGE AT DATE OF SCAN

A factor that might cause abnormalities to remain undetected is the fetal gestational age at which mothers were scanned. Table 11 shows how the unsuspected cases were distributed between four gestational age groups. The majority appear in the 16 week group: most of these mothers had only one scan during their pregnancies. The proportion of unsuspected cases fell as gestational age advanced.

DEATHS

Table 12 shows the number of deaths, how they occurred, and for what reasons. The necropsy rate was high so it was possible to ensure accurate pathological diagnosis. A third of all deaths were caused by termination of pregnancy and in 89.8% the antenatal diagnosis was confirmed at necropsy. Serious renal abnormalities often associated with multiple defects in other systems caused the majority of natural deaths.

Table 11 Number of babies with unsuspected urological abnormalities by gestational age at mothers', latest scan

	Gestational age (weeks)				Total
	≤16	17-20	21-30	≥31	
Total scanned	85	174	174	280	713
No unsuspected (%)	63 (74.1)	13 (7.5)	7 (4.0)	4 (1.4)	87 (12.2)

No record of scan date in 23 babies: four had unsuspected abnormalities.

Table 12 Deaths

Total deaths	179	24.3% of registered cases,
Necropsies	153 (85.5%)	0.7/1000 births
Terminations	59	
Necropsies	57 (96.6%)	
<i>Antenatal diagnosis</i>		<i>Postnatal diagnosis</i>
Neural tube, cystic hygroma, and other multiple defects including three chromosomal	21	All had urological defects
Polycystic disease	11	All confirmed
Bilateral renal dysplasia	8	7 confirmed, 1 normal
Bilateral renal agenesis	7	4 confirmed, 3 normal
Urethral valves and 'bladder neck obstruction'	8	All confirmed
Other urological including two prune belly	4	All confirmed
Antepartum, intrapartum stillbirths, spontaneous abortion	42	
Necropsies	37 (88.1%)	
<i>Antenatal diagnosis</i>		<i>Postnatal diagnosis</i>
Urological defects	23	16 confirmed, 6 normal, 1 unknown
Defects in other systems including three ascites	10	7 urinary, 3 normal (ascites)
Nil suspected	9	All urinary
Other deaths*	78	
Necropsies	61 (78.2%)	

*Severe urological defects and/or defects in other systems.

Discussion

The number of notifications per 1000 births in 1990 and the fact that the total number in that year was only marginally higher than the previous year probably indicates that recruitment of urological cases to the survey was virtually complete. The annual rise that occurred in previous years was probably due to a number of factors such as increasing awareness of the existence of the survey and the need to report cases of suspected fetal anomaly together with improvements in scanning equipment and expertise.

The implication in terms of surgery of suspected urological abnormalities antenatally is noteworthy. Of babies in whom renal dilatation was confirmed postnatally 44 were subjected to pyeloplasty and six to nephrectomy, 40 of these operations being performed at the ages of 6 months or less. Of 173 babies in whom upper urinary tract dilatation had been detected antenatally and urological abnormality confirmed postnatally, 93 (53.8%) required surgery.

The sex difference has been noted previously⁶ and is confirmed at a male:female ratio of 2:1. However, there was a significantly higher ($p=0.032$) proportion of males among the babies with obstructive urological abnormalities (excluding urethral valves) than in those with intrinsic renal parenchymal defects. This result accords with a previous observation that the highest incidence (66%) of urinary infections in infancy was in the first three months,¹² and that in this group there was a higher proportion of males who, furthermore, tended to develop infections earlier than females. Also, the incidence of obstructive uropathy was higher in males. In general terms, if a urinary tract abnormality is suspected, discerning the fetal sex could enhance accuracy.

Out of 583 cases in which a urological abnormality was suspected antenatally and 424 in which an abnormality was present postnatally the diagnosis was confirmed or correctly suspected in 292; this gives a sensitivity of 68.9% and positive predictive value of

50.1%. (If it is assumed from the total number of births in the region during the time period that the number of true negative diagnoses was of the order of thousands, specificity would be 99.9%: $X > 285 \times 0.9/0.1 = 2565$.) There was considerable variation in sensitivity between different diagnoses: for example of 113 babies who had confirmed hydronephrosis, the diagnosis was correctly suspected in 97; this gives a sensitivity of 85.8%, specificity of 48.2%, a positive predictive value of 23.3%, and a negative predictive value of 94.9%. In 33 babies with bilateral renal agenesis 18 were correctly predicted with a further six reported because of intrauterine growth retardation; a combined sensitivity of 72.7% and specificity 98.9%. The contrary was found with posterior urethral valves: of 26 cases found postnatally only six were suspected antenatally, this gives a sensitivity of 23%, and specificity of 98.7%. Of 12 cases suspected antenatally five, including one female, were normal and another had hydrocolpos.

Calculations from the figures given by the authors of a previous study of a series of 6360 pregnancies of which 6292 were scanned and in which an attempt was made to discover false negative diagnoses, reveal a diagnostic sensitivity of 85.7%, specificity 99%, and positive predictive value 45.7% (due to the lower prevalence).¹³ The higher sensitivity level illustrates the effect of basing a study on a single hospital maternity department.

Among babies with unsuspected abnormalities six with unilateral renal dysplasia died, four because of multiple abnormalities in other systems and two from pulmonary hypoplasia. Two other babies required peritoneal dialysis and four were surviving with other serious abnormalities. Seven of the babies with unilateral renal agenesis died; one was aborted spontaneously and the others had serious abnormalities in other systems including chromosomal, cardiac, and diaphragmatic. Two other babies had oesophageal atresia and one had rectal agenesis. Two babies with urethral valves died (one antepartum stillbirth and one at 1 week of age) as did all the babies with bilateral renal agenesis: four with polycystic kidneys died from pulmonary hypoplasia and two with bilateral renal dysplasia died because of multiple defects elsewhere. One baby with multicystic kidney also had a chromosomal defect and aborted spontaneously and one baby with ectopia cloacae was successfully repaired surgically at 1 week, the other died. Both babies with urethral atresia and the babies with absent bladder, bladder neck obstruction, bladder rupture, and prune belly all died. The mortality rate in this group was 39.6%, substantially higher than the overall mortality; furthermore, the incidence of serious abnormalities in other systems was also high and it is surprising that they were not suspected.

It is evident that a large majority of unsuspected abnormalities occurred in the babies whose mothers had only one antenatal ultrasound scan at or before 16 weeks. This supports the recommendation of the Joint Study

Group on Fetal Abnormalities that mothers should, whenever possible, be offered two scans: a dating scan at 16 weeks and an anomaly scan by 20 weeks.¹⁴ It was also clear that some urological abnormalities—for example ureteric reflux, are unlikely to be suspected unless mothers are scanned as late as the mid third trimester.

This series has shown that with the cooperation of consultants and specialists in differing fields throughout a region it is possible to establish a fetal abnormality survey that can provide valuable epidemiological and audit data; an increasingly essential component of health care management.

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