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Isolated fetal pyelectasis: assessment of risk for postnatal uropathy and Down syndrome

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ABSTRACT

Eighty-two consecutive fetuses with ultrasound evidence of isolated pyelectasis (defined as dilatation in the anteroposterior renal pelvic dimension of ≥ 4 mm) were prospectively followed to determine the risk for postnatal uropathy and Down syndrome. In 98 (60%) kidneys, isolated pyelectasis was shown to be the first manifestation of a pathophysiological process that evolved into a gamut of postnatal uropathies (defined as urological conditions requiring remedial surgery or extended medical surveillance). Data quantifying the risk for postnatal uropathy in fetuses with varying degrees of isolated pyelectasis, at different gestational ages, are presented in figure format to facilitate prenatal counselling. Bivariate analysis showed that the evolution of isolated pyelectasis to uropathy was statistically significant when in utero *progression was noted or in conjunction with other findings including contralateral pyelectasis (p < 0.01), male gender (p < 0.01) and increased kidney length (p < 0.001). Importantly, 55% of the infants requiring corrective surgery demonstrated* in utero *progression of pyelectasis (p < 0.002). Serial ultrasound examinations were necessary to evaluate progression or regression in the extent of pyelectasis. Finally, isolated pyelectasis was associated with an increased risk for Down syndrome, beginning at maternal age of 31 years, in the interval of 16–20 weeks' gestation.*

INTRODUCTION

Counselling prospective parents regarding an ultrasound finding of isolated fetal pyelectasis is difficult, because the etiology is not apparent. Furthermore, published studies regarding the outcome of fetuses with isolated pyelectasis do not demonstrate a clear consensus. For example, Arger and colleagues[1] suggested that pyelectasis may be associated with significant hydronephrosis when the anteroposterior diameter of the renal pelvis is > 10 mm. However, other investigators[2] have reported that pyelectasis may be associated with hydronephrosis when the anteroposterior diameter of the renal pelvis is ≥ 4 mm or ≥ 7 mm, before and after 33 weeks' gestation, respectively. The association between isolated fetal pyelectasis and Down syndrome is also controversial. Specifically, isolated pyelectasis is shown to be associated with a three-fold increase in chromosomal abnormalities over the maternal age-related risk[3]. On the other hand, Corteville and coworkers[2] indicated that the risk for Down syndrome in fetuses with isolated pyelectasis was only 1 : 340 – a risk that does not warrant amniocentesis for assessment of fetal karyotype. The present study was undertaken to examine further the risk for postnatal uropathy and Down syndrome in fetuses with isolated pyelectasis.

MATERIALS AND METHODS

Consecutive fetuses with ultrasound diagnosis of isolated pyelectasis (dilatation of the anteroposterior diameter of the renal pelvis to a dimension ≥ 4 mm) were prospectively evaluated from 1 July 1988 until 31 July 1993. Postnatal urological follow-up was carried out by one pediatric urologist (M.M.) at the Children's Memorial Hospital.

In all fetuses, gestational age was determined by accepted methods, including a reliable dating of the last menstrual period and measurement of the first-trimester crown–rump length and biparietal diameter from 14 to 26 weeks' gestation. Amniotic fluid volume was assessed by the amniotic fluid index[4].

The features monitored in both prenatal and postnatal scans included: extent of pyelectasis as determined by the anteroposterior width of the renal pelvis, progression or regression of pyelectasis, development of hydronephrosis (defined as pyelectasis with caliectasis), ureterectasis (ureteral dilatation of any width), persistent bladder dilatation,

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exceeding the normal average diameter of 2 cm and 3 cm in the second and third trimesters of pregnancy, respectively, and kidney length. The normal variation in kidney length was derived from our data by the following formula: kidney length (mm) = gestational age (weeks) + 7.2 (95% CI ± 10).

Ultrasound examination of newborns with a normal physical examination was delayed 48 h to avoid imaging during the interval of physiological oliguria. This was essential because the oliguric phase is associated with an artificial 'underfill' of the upper urinary tract and could result in a false normal appearance[5].

Newborn urological management was individualized in relation to the nature of the abnormality. When the findings on a sonogram of the affected newborn suggested no need for immediate care, subsequent evaluation was deferred for at least 1 month. At that time, the extent of pyelectasis, ureterectasis or bladder dilatation was determined by ultrasound examination and was graded in a standard manner[6,7]. In addition, the drainage capacity of the kidneys was monitored by the 'well tempered' renogram (WTR)[8]. A voiding cystourethrogram was used to diagnose bladder neck obstruction or vesicoureteral reflux, and a 'scout' film of the abdomen was obtained to rule out spina bifida occulta. Conversely, treatment was instituted immediately following birth in newborns with ultrasound evidence of uropathy due to obstructive disease, including urine ascites or posterior urethral valves. Confirmation of obstruction was based on the surgical diagnosis of a stricture or kink of the ureter and histopathological evidence of obstruction[9].

The outcome was classified as uropathological in all infants who required extended follow-up. This encompassed infants who underwent remedial surgical procedures as well as those who needed continuing medical surveillance to evaluate, for example, the grade of reflux. Medical surveillance was also necessary to monitor the infants for onset of bacteriuria associated with stasis of urine in the renal pelvis.

Prenatal urological ultrasound findings were compared statistically with postnatal outcome. Continuous pre- and postnatal data were analyzed by Student's *t*-test and by comparison of linear regression lines. The χ^2 test was performed to evaluate measures involving integral data. Predictors most strongly associated with abnormal outcome were entered into logistic models to predict postnatal outcome by stepwise entry of predictors. Computer entry of data was carried out with software provided by the Society for Fetal Urology as part of a national collaborative pediatric urological effort[10]. Statistical analysis was performed by means of True Epistat software (Richardson, TX) and SPSS ver6.0 (Chicago, IL).

The prevalence of Down syndrome in the population scanned was estimated by use of the *a priori* risk at our center (1 : 393). The sensitivity and specificity of the marker (isolated pyelectasis) were calculated. Subsequently, Bayes' theorem was applied to derive the adjusted risk for the disease (Down syndrome) based on the *a priori* risk, relative to both maternal age and gestational age[11,12]. In Bayes' theorem, the probability of disease (trisomy 21), given a positive test (isolated pyelectasis), is the product of the probability of a positive test in a given disease (sensitivity) and the probability of disease (prevalence or *a priori* risk) divided by the probability of a positive test; it is expressed by the formula:

$$\text{Sensitivity} \times \textit{a priori}\ \text{risk}/[\text{sensitivity} \times \textit{a priori}\ \text{risk} + (1 - \text{specificity}) \times (1 - \textit{a priori}\ \text{risk})].$$

The denominator of the formula defines the probability of a positive test[11].

RESULTS

Over the course of this 5-year study, 11 340 pregnancies were ultrasonographically examined during the second and third trimesters and 82 fetuses (0.72%) showed isolated pyelectasis. The mean gestational age at diagnosis of isolated pyelectasis was 26 weeks (range 17–39 weeks). Urological tests on liveborns were performed beginning at a median age of 1.5 weeks, with last follow-up at a median age of 1 year (range up to 4 years).

In 98 (60%) kidneys, the pathophysiological process of pyelectasis evolved into a gamut of postnatal uropathies (Table 1). There was considerable overlap in the anteroposterior width of the renal pelvis in groups with normal or uropathological outcome (Figure 1a). The likelihood of postnatal uropathy, relative to the extent of pyelectasis at different gestational ages, is shown in Figure 1b. In some kidneys, regression in the anteroposterior width of the renal pelvis to a dimension of ≤ 3 mm was noted (Figure 1b). In such fetuses, the risk for postnatal uropathy was low, but still present (Figure 1b).

Postnatal uropathological outcome included 43 kidneys with pyelectasis that could not be attributed to obstruction

Table 1 Postnatal uropathological outcome in 82 fetuses* with ultrasound diagnosis of isolated pyelectasis†

Outcome	*n*	%
Non-obstructive pyelectasis	43	44
Hydronephrosis secondary to ureteropelvic junction obstruction	27	28
Multicystic kidney	3	3
Hypodysplastic kidney	4	4
Non-functioning kidney‡	1	1
Posterior urethral valves	4	4
Vesicoureteral reflux	4	4
Ureterocele	1	1
Ureterectasis	1	1
Non-obstructive megaureter	6	6
Ectopic ureter	2	2
Dilated bladder	2	2
Total uropathy**	98 (60% of 162 kidneys*)	

*Excludes one fetus with bilateral isolated pyelectasis and Down syndrome – pregnancy was terminated; †defined as unilateral or bilateral isolated dilatation of renal pelvis with anteroposterior diameter of ≥ 4 mm; ‡it is believed that pyelectasis evolved into Potter type IIB kidney in which renal tissue would only be visible microscopically; **uropathological outcome included infants requiring remedial surgery or extended medical surveillance (see text)

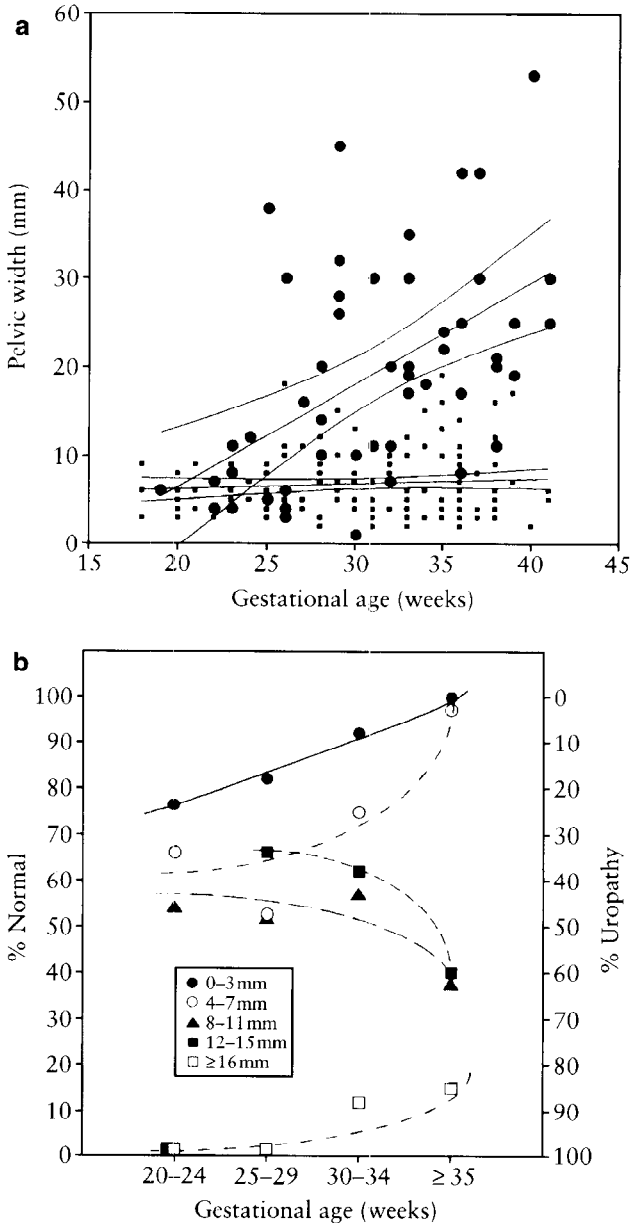

Figure 1 (a) Distribution in extent of prenatal non-specific pyelectasis relative to gestational age and normal vs. uropathological postnatal outcome. Note the overlap between the two groups. The diagram does not predict the likelihood of uropathological outcome. Regression equations: non-obstructed (squares), $y = 5.10 + 0.06x$; obstructed (circles), $y = -16.56 + 1.15x$. (b) The likelihood of uropathological outcome determined for five levels of pyelectasis at different gestational ages. The diagram can be used to counsel prospective parents because it enhances visual appreciation of the risk involved. Note the uropathological outcome in approximately 25–35% of kidneys when the anteroposterior diameter of the renal pelvis falls in the range of 4–7 mm, prior to 35 weeks' gestation. Additionally, uropathological outcome is noted in approximately 5–22% of kidneys when the anteroposterior diameter of the renal pelvis regresses to the range of 0–3 mm, prior to 35 weeks' gestation.

or clinically significant reflux (Table 1). Specifically, in each of these infants serial ultrasound examinations showed normal size of kidneys and no ureterectasis. Furthermore, urinary tract infection was not detected on follow-up. Thus, the etiology of pyelectasis remained idiopathic in these fetuses.

Serial prenatal ultrasound examinations were performed on 105 kidneys. The anteroposterior width of the renal pelvis showed progression in 35 (33%), regression in 26 (25%) and no change in 44 (42%). Postnatal uropathy was noted in 21 (60%), six (23%) and 14 (32%) of the kidneys showing progression, regression, or no change in the anteroposterior width of the renal pelvis, respectively. When progression of pyelectasis occurred prenatally, the probability of corrective surgery in the infant was 50%. In fact, 55% of the infants requiring corrective surgery showed *in utero* progression in the extent of pyelectasis ($p < 0.002$). Bivariate analysis also showed that evolution in fetal isolated pyelectasis to uropathy was more likely to occur when *in utero* progression was noted ($p < 0.01$) (Figure 2), or in conjunction with other findings, including contralateral dilatation ($p < 0.01$), male gender ($p < 0.01$), and increased kidney length beyond the upper limit of normal ($p < 0.001$). Additionally, the presence of isolated pyelectasis along with increased kidney length was significantly predictive of postnatal obstructive uropathy requiring surgical intervention ($p < 0.0001$).

Other results included (1) reduced postnatal renal function in five of seven obstructed kidneys in which the renal pelvic diameter (mm) was greater than the gestational age (weeks); (2) increase in the odds of corrective postnatal surgery (8 : 1) in fetuses with an anteroposterior renal pelvic width of > 15 mm in the gestational interval of 20–25 weeks; and (3) greater risk for postnatal ureteropelvic junction obstruction if ureterectasis was visualized on any scan following the first one.

Isolated pyelectasis was also associated with trisomy 21 in three of 82 such fetuses. In the first case, the diagnosis was made prenatally and the pregnancy was terminated. In two other women, 19 and 34 years of age, trisomy 21 was diagnosed in the neonate. Neither triple screen nor α-fetoprotein testing was performed on these women. The fetal karyotype was normal in 32 pregnancies in which amniocentesis was performed. The phenotype was normal in the remaining 47 infants.

Since the prevalence of trisomy 21 in the observed population at our referral center is 1 : 393, we estimated a total of 28 fetuses with Down syndrome and no pyelectasis (11 258/393). We then established the sensitivity (3/31) and specificity (11 230/11 309) for the marker (isolated pyelectasis). Subsequently, Bayes' theorem was applied to derive the adjusted risk for trisomy 21 (in the presence of pyelectasis) based on specific *a priori* risks estimated by maternal age and gestational age[11,12] (Table 2).

DISCUSSION

Our longitudinal observations show that isolated fetal pyelectasis frequently represents the first manifestation of a urinary tract abnormality, the pathophysiology of which evolves into a range of postnatal uropathies (Table 1). The correlation between the extent of prenatal isolated pyelectasis and postnatal urological outcome has allowed us to

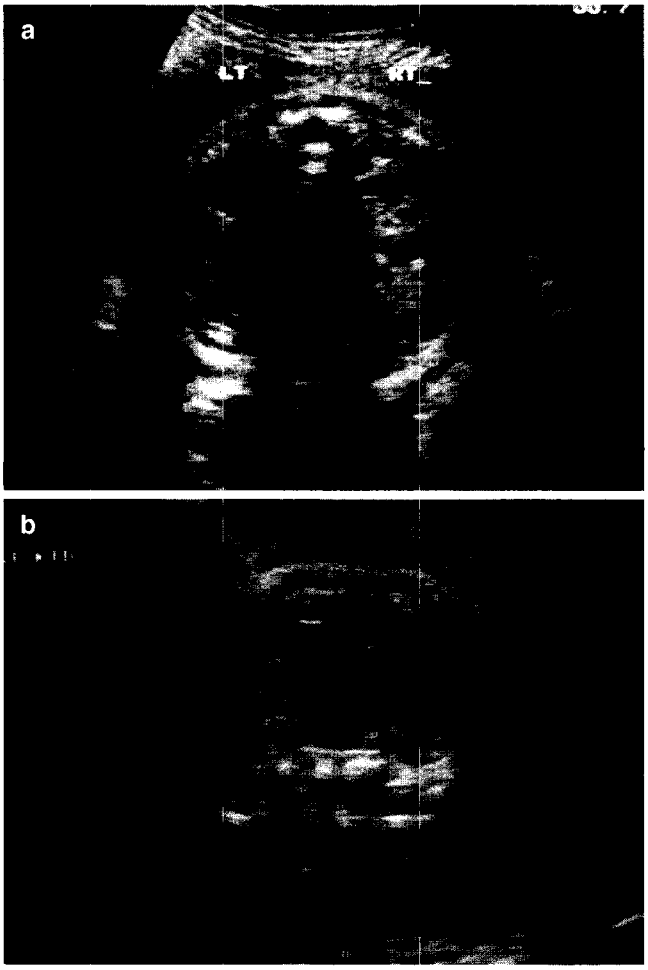

Figure 2 Ultrasound images illustrating progression in prenatal isolated pyelectasis predictive of uropathy. (a) Fetal ultrasound image at 22 weeks' gestation, showing pyelectasis (7 mm) in left kidney, yielding a 35% risk for uropathy. (b) Coronal view at 32 weeks' gestation showing left hydronephrosis and increase in kidney length to 64 mm. Normal for this age is 39.2 ± 10 mm (see text). Amniotic fluid analysis showed a normal male. These fetal findings of progression in the extent of pyelectasis, increased kidney length and male gender are predictive of postnatal uropathy (see text). The infant underwent pyeloplasty for ureteropelvic junction obstruction

forecast the likelihood of uropathy in any given fetus (Figure 1b). The data in this figure are stratified by the width of the anteroposterior diameter of the renal pelvis at various gestational ages. The illustration serves to facilitate prenatal counselling, because the potential risk becomes readily apparent to the prospective parents. It can be explained, for example, that, in a 25–29-week fetus with isolated pyelectasis of 4–7 mm, the chance of postnatal uropathy will be 38%.

It can also be explained that progression in the extent of isolated pyelectasis significantly increases the risk for postnatal structural abnormalities that require corrective postnatal surgery. On the other hand, regression in the anteroposterior width of the renal pelvis lowers the risk for postnatal uropathy (Figure 1b). This decreased risk can be attributed to three factors:

(1) Diminution in the obstructive effect of the ureteral folds of Ostling[13];

(2) Resolution of mild posterior urethral valves; and

(3) Reduction in vesicoureteral reflux, due to better valvular competence.

Additionally, ultrasound visualization of ureterectasis, on any scan subsequent to the first one, increases the risk for postnatal ureteropelvic junction obstruction. It is possible that delayed or faulty recanalization of the ureteropelvic junction is etiological in the pathoembryology of this type of obstruction[14].

The scope of prenatal counselling may be further widened by a discussion of two other areas. The first is that of postnatal non-obstructive pyelectasis. Specifically, in 44% of the uropathological kidneys (Table 1), the etiology of pyelectasis remains uncertain, since neither obstruction nor clinically significant reflux was noted on follow-up examinations. In addition, urinary tract infections did not occur. It should be emphasized, however, that urological surveillance of all these infants is mandatory to ensure absence of any of these complications.

The second is related to the terminology of 'minimal hydronephrosis'. Since 1985, when Arger and colleagues[1]

Table 2 Estimated* (Est) and adjusted (Adj) risks for trisomy 21 (1/number) based on maternal age and gestational age in structurally normal fetuses, as modified by ultrasonically diagnosed pyelectasis

Maternal age (years)	*Gestational age* (weeks)									
	16		*20*		*25*		*30*		*35*	
	Est	*Adj*	*Est*	*Adj*	*Est*	*Adj*	*Est*	*Adj*	*Est*	*Adj*
20	1053	932	1175	1039	1294	1145	1388	1388	1464	1464
28	768	419	856	503	943	554	1012	723	1068	844
29	695	347	776	431	855	502	917	611	967	705
30	617	308	688	351	758	421	813	593	858	626
31	536	191	597	213	658	335	706	360	745	413
32	455	162	507	181	599	357	599	357	632	448
33	378	90	421	150	464	165	498	178	525	187

Note that the traditional risk for Down syndrome (1 : 250 at maternal age of 35 years) is used to counsel patients regarding the possibility of testing to determine fetal karyotype. The tabulated risks above show that the increase, beyond the traditional risk for Down syndrome, begins at maternal age of 31 and 32 years, in the gestational interval of 16 to 20 weeks. In comparison, the risk is increased at all gestational intervals in women 33 years of age or older; *estimates of risk are adapted from reference 12

suggested that pyelectasis with an anteroposterior diameter of > 10 mm is predictive of significant hydronephrosis, 'minimal hydronephrosis' has come to mean pyelectasis with an anteroposterior diameter of < 10 mm. Such terminology may no longer be applicable, because isolated fetal pyelectasis can evolve into a spectrum of urinary tract pathology other than hydronephrosis. Additionally, the terminology may be misleading, because it implies inconsequential outcome – contrary to our findings and those published in a recent report[2]. Use of the term hydronephrosis also erroneously suggests that pyelectasis cannot exist by itself and is always associated with caliectasis.

The terminology of minimal hydronephrosis may also downplay the risk for Down syndrome in such fetuses. We show this risk to be related to the estimated prevalence of trisomy 21 relative to both maternal age and gestational age[12] (Table 2). Specifically, the risk for Down syndrome is increased (beyond the traditional risk of 1 : 250 at maternal age of 35 years) in women 31 or 32 years of age, during weeks 16–20 (Table 2); further, the risk is increased at all gestational intervals, in women 33 years of age or older. At 16 weeks' gestation, a triple scan rather than a maternal age risk for trisomy 21 can also be used. For example, in a 31-year-old woman at 16 weeks' gestation and a triple screen risk of 1 : 536, the adjusted risk for trisomy 21 would still be 1 : 191 (Table 2). The results of this study are in some agreement with the report by Nadel and colleagues[15]; these authors revised their scoring method to include pyelectasis as a criterion that increases risk for autosomal trisomy in women 33 years of age or older. Our data are different, however, in that the increased risk for Down syndrome begins at a maternal age of 31 years (Table 2).

Finally, the fact that isolated pyelectasis can result in uropathy, regardless of whether an increase or a decrease in the size of the renal pelvis occurs, underscores the need for serial ultrasound studies to evaluate the evolving pathophysiology of this condition. It also suggests that the 4-mm cut-off defining the normal anteroposterior width of the renal pelvis may be quite arbitrary and should be the subject of further investigation.

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