

Late second trimester assessment of pyelectasis (SERP) to predict pediatric urological outcome is improved by checking additional features

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Abstract

Objective. Counseling for pyelectasis in the late 2nd trimester is usually based only upon assessing the antero-posterior (AP) width of the renal pelvis. We hypothesized that checking additional features would better predict postnatal outcome.

Study design. Ultrasound (<24 weeks gestational age (GA)) and newborn outcome data collected prospectively since 1986 were analyzed retrospectively. We determined if outcome predictions in kidneys with a sonographically evident renal pelvis (SERP), which had evaluation of additional features (e.g., renal and bladder lengths, presence of a dilated ureter or dilated calyces) are more accurate than those that did not have these features.

Results. There were 286 fetuses studied with pediatric follow-up of an average of 6.5 years. There were 338 exams providing 459 ultrasound images with SERP. Additional features were not assessed in 183 fetuses; however 103 fetuses did have evaluation of additional features. These features were categorized as abnormal (92) or as normal (11). Fetuses with SERP and abnormal additional features required extensive urological care or died 6.1 times more often than fetuses in which additional features were not examined ($p < 0.001$) and 12.9 times more often when additional features were normal ($p < 0.001$).

Conclusion. Fetal kidneys with SERP (<24 weeks GA) and an abnormal additional ultrasound feature had extensive pediatric care significantly more often than when such features were not evaluated or were normal.

Keywords: *Pyelectasis, outcome, prenatal diagnosis, pediatrics*

Introduction

Maternal/parental counseling regarding fetal sonographic findings is important to coordinate and extend obstetric and pediatric care. When what has been termed 'pyelectasis' is encountered on prenatal imaging studies, this counseling involves forecasting of newborn urological outcome and is currently done by correlating the magnitude of antero-posterior (AP) width of the renal pelvis with postnatal outcomes. The predictive value of several levels of this measurement (e.g., ≥ 4 , ≥ 7 , or ≥ 10 mm) has been researched at various intervals of gestation, but the current literature on prenatal diagnosis of renal

pyelectasis is inconsistent with respect to recognizing a diagnostic threshold to predict neonatal urologic outcome. Significance is cited variably between 4 and 10 mm as a critical threshold for predicting postnatal urinary obstruction such as hydronephrosis (HN) or vesicoureteral reflux. The impact of gestational age upon these thresholds has not been fully determined. Because the significance of dilatation in the renal pelvic width is uncertain, we view the term pyelectasis itself as problematic because it inherently labels a case as 'abnormal' when the finding may be a normal variant and be associated with a normal outcome. Because this label fosters misconceived clinical attitudes, we introduce the term SERP, as an

acronym for sonographically evident renal pelvis, which may help to clarify these misconceptions. Herein, the term SERP is substituted for the term pyelectasis.

Pediatric ultrasonographic features recognized to be pertinent to urological diagnosis have not been extensively researched for fetal ultrasonographic pertinence. These additional features include: enlarged renal length, calyceal dilatation, progression of renal dilation, duplex pelvis, imaging of the normally non-visualized ureter, and enlarged bladder size. These additional features are important because they may be markers of maldevelopment. For example, enlarged renal length may result from obstructed urine drainage noted in ureteropelvic junction (UPJ) obstruction. Calyceal dilation in conjunction with SERP may represent obstruction noted in pediatric hydronephrosis. Duplex renal pelvis is noted in cases of ureteral ectopia (i.e., primarily upper pole dilation) or lower pole UPJ obstruction (i.e., primarily lower pole dilation), and enlarged bladder size frequently accompanies vesicoureteral reflux (VUR). Therefore, it is plausible that such fetal urological features additional to SERP may be clues to defining clinical significance.

As the pattern of SERP (e.g., pyelectasis, hydronephrosis, or renal duplication), enlarged renal length and bladder size have not been previously examined for correlation with outcome, we examined the possibility that these features show significance additional to that of SERP alone. We researched this question for cases with fetal diagnosis between 15 and 24 weeks of gestation, as this is the most common interval for a fetal urological finding to have been first detected and also because this group has not previously been well studied. We hypothesized that assessing kidneys and bladder for additional features described above would better predict postnatal outcome than monitoring extent of SERP alone.

Materials and methods

Study design

IRB approval was obtained for the performance of this study. This was a retrospective case-control study. The control group was comprised of fetuses with ultrasound images that measured extent of SERP but had not been studied for additional features, and the study group was comprised of fetuses with ultrasound images that measured the extent of SERP and evaluated other additional features. The study group was categorized into two subgroups: (1) those with normal additional features and (2) those with abnormal findings.

Since 1986 the authors (MD, RES, EW, NG, DG) have followed the outcome of consecutive

pregnancies referred for tertiary care urological evaluation (MM) of fetal urological anomalies to the Division of Urology, Children's Memorial Hospital, Chicago. The findings in these cases have been shared by prenatal and postnatal caregivers at regularly held departmental conferences and/or by personal communications. All fetal ultrasound exams were performed by a registered diagnostic medical sonographer who was supervised by a maternal-fetal medicine specialist. Gestational age was determined by the best obstetrical estimate.

Inclusion criteria

In this report, cases with prenatal ultrasound between 15 and 24 weeks gestational age (GA) showing SERP without a specific diagnosis and with newborn follow-up data were examined for postnatal outcome. The ultrasound exams were grouped as SERP without checking done for additional features (control group) and SERP with additional features checked (study group) for: pattern of SERP (i.e., pyelectasis alone, hydronephrosis, or renal duplication), renal polar and bladder sagittal lengths. Once SERP was appreciated, follow-up sonography was done at the discretion of the maternal-fetal medicine specialist.

Definitions of additional ultrasound features

For the 2nd trimester, elongated kidney length was extrapolated from published normative data [1]. As a practical approximation, the upper limit of normal polar length (mm) \leq gestational age (GA) (weeks) +5. Hydronephrosis was diagnosed if there was dilation of a major calyx along with SERP \geq 4 mm. This compares to the pediatric ultrasound definition of hydronephrosis, which includes uniform dilation of the minor calyces [2,3]. A kidney with SERP may have progress to hydronephrosis, or hydronephrosis may have been seen *ab initio*. A kidney was categorized as a duplicated kidney if there was asymmetric size of the bifid renal pelvic moieties. This definition did not encompass a kidney that was completely duplicated and affected symmetrically by VUR to each moiety. This omission appears acceptable as this circumstance has yet to be encountered by the cumulative experience of the authors. A ureter was categorized as a dilated ureter if it was imaged by ultrasound beyond the renal pelvis at any gestational age. A bladder was categorized as an enlarged bladder if the sagittal length was elongated above the upper limit of normal (i.e., elongated bladder sagittal length (mm) \geq GA in weeks +2) [4]. SERP progression was operationally diagnosed if the extent of SERP was $>$ 4 mm more than the exam done a month earlier.

Prenatal obstetric care including the interval of fetal ultrasound examination and termination of pregnancy was structured by the referring obstetric caregivers.

Fetal cases excluded

Cases were excluded if the fetal ultrasound done by 24 weeks of gestation showed an anomaly whose outcome was already predictable: (1) a specific anomaly (e.g., ureterocele, multicystic kidney), (2) SERP that was not an isolated finding (e.g., associated with myelomeningocele), or (3) an abnormal kidney that was not dilated (e.g., echogenic) (Table I). Fetal cases with known aneuploidy were excluded. The normal twin of an affected fetus was not included in this analysis.

Postnatal evaluation

Postnatal care was structured by one author (MM). All newborns included in the study had a urine examination for infection and a follow-up ultrasound, typically by 10 days after birth unless the fetal findings showed bilateral hydronephrosis in which case evaluation was initiated in the newborn period. The results of these tests guided the performance of the subsequent evaluation which was either follow-up by phone interview at a year of age or by performing one or several of the following tests: periodic sonography (done after 10 days old), well tempered diuretic renography (WTR) (done after 1 month old) [5], furosemide enhanced sonography (after 3 months old), and/or voiding cystourethrography (VCUG).

Renal obstruction was diagnosed when the WTR showed delay of lasix induced drainage of MAG3 (99Tc-mercaptoacetyltriglycine, Mallinckrodt) from

the renal pelvis as ureteropelvic junction obstruction (UPJO) or ureter as ureterovesical junction obstruction (UVJO), and delay was accompanied by a post WTR-ultrasound showing pathological dilation. Retrograde/antegrade pyelography was done as necessary to secure a diagnosis before surgery was pursued. Azotemia was diagnosed as elevation in serum creatinine above predicted normal for age. Intravenous pyelogram (IVP) was done to evaluate complex anatomy.

Children with minimal dilation had follow-up information obtained from the child's pediatric caregiver.

Outcomes

The outcomes were categorized by whether the postnatal condition of the baby involved, in addition to a postnatal ultrasound, slight or extensive urological care needs. Slight urological care involved periodic urine examinations until 1 year of age, but not involving: administration of medication, performance of invasive tests, or surgery; extensive urological care involved performance of invasive tests (e.g., WTR or VCUG), urological follow-up done beyond 1 year of age, or if surgery was performed.

For cases with extensive urological care, the urological parameters were examined radiographically. Renal and bladder architecture were examined by ultrasound. Kidney percent differential renal function and drainage were examined by diuretic renal scan. The status of vesicoureteral reflux was established by VCUG or by the ultrasound finding of an immediate increase in renal pelvic dilation immediately post void.

Pediatric urological surgery was done to relieve obstruction or remedy VUR. Surgery to address obstruction included: pyeloplasty for UPJO, reimplantation of ureter in UVJO, or transurethral resection/ablation of posterior urethral valves (PUV); ureteral reimplantation was done to correct vesicoureteral reflux. The performance of postnatal surgery was determined by current empiric pediatric urological practice, which is exclusively based upon the results of the above radiographic tests and urine infection status along with parent and pediatric caregiver preferences. The 'performance' of surgery is not equivalent to the 'need' for surgery, as this cohort was comprised of children who were clinically well [6]. Cases with hydronephrosis in which obstruction was diagnosed but whose families chose not to elect surgery are categorized as showing extensive urological needs.

Statistical analysis

The fetal and newborn data were entered prospectively into a computer database. Fetal and postnatal

Table I. Cases excluded because specific ultrasound diagnoses were made during the second trimester.*

Reasons for exclusion	No.
Multicystic kidney disease	20
Cyst/dysmorphic/echogenic	13
Ureterocele	10
Renal duplication	3
Absent kidney	3
Cloaca/bladder exstrophy	3
IPCKD	2
Megacystis without hydronephrosis	2
Hydronephrosis with omphalocele	1
Prune belly syndrome	1
Total	58

*These cases were excluded as the pediatric outcomes were already recognized. Also excluded were cases with no follow-up ($n=19$) and cases with ultrasound data retrieved after the newborn presented with illness ($n=5$). IPCKD, infantile polycystic kidney disease.

data were analyzed as noted in the study design (see above). Preliminary analyses of continuous data were conducted using *t*-tests to compare means between two groups, and nominal outcomes were evaluated using Chi-square tests.

The main comparisons were between the three groups: (1) control group – SERP without evaluating for additional features, (2) study group – SERP with evaluating for additional features, which are abnormal, and (3) study group – SERP with evaluating for additional features, which are normal. The primary outcome was need for extensive or slight urological care. While outcome was at the fetus level, the primary predictor was ultrasound data. For some fetuses, there were multiple ultrasounds per kidney over the study duration, and some fetuses had bilateral involvement.

To address the repeated measures data, generalized linear models were used to determine whether assessing for additional features was associated with better prediction of the need for extensive or slight urological care. This allowed us to account for clustering of ultrasounds by fetus. If the overall test between the three groups was statistically significant, pairwise comparisons were conducted. Results are expressed as odds ratios for the likelihood of needing ongoing care, with the corresponding 95% confidence intervals. Conclusions were made at the 0.05 level of significance. Data analyses were conducted using SAS analysis software version 9.1.

Results

Between January 1986 and January 2005 there were 1300 pregnancies referred for evaluation. From this group there were 368 pregnancies that had a first ultrasound performed between 15 and 24 weeks GA. There were 286 fetuses whose ultrasound exams showed SERP without a specific diagnosis and are the subject of this study. The remaining 82 fetuses were excluded due to: diagnosis of a specific fetal anomaly, lack of follow-up, or normal prenatal ultrasounds with postnatal presentation for pediatric care (Table I).

The mean maternal age was 31.8 years (± 5 SD, median 28 years, range 17–44 years). Pediatric follow-up was for an average of 18 months (median 12.8 months, SEM 1.4 months, range 1 day–15 years). There were no pregnancies with more than one fetus affected.

Ultrasound findings additional to SERP, by fetus

The 286 fetuses included in this study underwent 1–3 ultrasound exams between 15 and 24 weeks GA for a total of 338 exams. The exams showed additional features: not evaluated in 183 fetuses,

evaluated and abnormal in 92 fetuses, or assessed and normal in 11 fetuses.

Ultrasound findings additional to SERP, by kidney image

The 338 exams showed 459 ultrasound images of kidneys affected by SERP. There were 153 fetal kidney images that showed SERP, and of the additional features checked 137 were abnormal and 16 were normal. As one image may show more than one additional feature there were a total of 212 additional features (Table II). There were 306 kidney images not assessed for additional features.

Comparison of newborn urological outcome predictions of SERP with and without evaluating for additional ultrasound features

The following percentages are presented in order to compare differences in outcome prediction when additional features are assessed. This calculation was done using data from the last ultrasound exam performed at <24 weeks GA, as this time period was the last opportunity for the family to exhibit choice in pregnancy completion (Table III).

Fetuses who showed abnormal additional features requiring extensive urological care needs (89%), required these needs 6.1 (95% CI: 3.1, 11.9) times more often than fetuses in which additional features were not checked (52%) ($p < 0.001$). The specific nature of extensive care provided is shown in Table III.

Fetuses who showed normal additional features and who required extensive urological care (36%), required this care 12.9 (95% CI: 3.5, 48) times less often than fetuses showing abnormal additional features (89%) ($p < 0.001$).

Table II. Incidence of additional ultrasound features noted in kidneys.

Additional feature noted*	No.
Normal	
Kidney length normal	15
Bladder length normal	3
Sub-total	18
Abnormal	
Hydronephrosis	50
Kidney length elongated	99
Bladder enlarged	25
Ureter dilated	9
SERP progresses/SERP progresses to hydronephrosis	8
Kidney duplicated	3
Sub-total	194
Total	212

*There may be more than one additional feature noted per kidney.

Table III. Comparison of newborn* urological outcomes of SERP without and with evaluating for additional ultrasound features.

Newborn urological outcomes	SERP and additional feature			Total
	Additional feature not assessed	Additional feature normal	Additional feature abnormal	
Needs slight	88 (48%)	7 (64%)	11 (11%)	106
Needs extensive for:	95 (52%)**	4 (36%) [†]	81 (89%)** [†]	180
Surgery	40 (42%)	2 (50%)	54 (67%)	
Hydronephrosis	31 (33%)	1 (25%)	6 (7%)	
Solitary kidney	2 (2%)		12 (15%)	
VUR	19 (20%)	1 (25%)	6 (7%)	
Death			3 (4%)	
UTI	3 (3%)			
Subtotal		11	92	
Total	183		103	286*

*Total number of fetuses. **[†]Indicate comparisons that show statistical significance (see results). VUR, vesicoureteral reflux; UTI, urinary tract infection.

Fetuses who showed normal additional features who required extensive urological care (36%) tended to require this extensive urological care 2.12 (95% CI: 0.63, 7.1) times less often than fetuses in which additional features were not checked (52%) ($p = 0.23$).

Figures 1–3 illustrate these observations and demonstrate the evaluation of additional features and how this information may influence parental counseling.

Discussion

There is wide acceptance that diagnosis of fetal urological anomalies is important to intrapartum maternal and postnatal newborn managements. Methods to predict outcome of newborns who show a dilated fetal urinary tract have steadily become of increasing interest since the report of Arger et al. [7] over 15 years ago. Numerous subsequent reviews have sought to ascertain the extent of AP SERP, which has clinical relevance to postnatal outcome. Today, the cutoff levels of significance suggested by Corteville et al. are largely still applied to predict outcome: ≥ 4 mm before 33 weeks and ≥ 7 mm after 33 weeks GA [8]. Yet, it is recognized that lower levels of dilatation may also be clinically important and merit newborn follow-up [9], while higher levels of fetal dilatation may show a normal pattern in the newborn. For this reason we suggest the acronym SERP, which does not connote that urine evident in the renal pelvis is inherently pathological. The sonographic finding should not be viewed as ‘dilatation’, but rather may simply represent an appearance within the range of normal. Furthermore, we refined the method of assessing the meaning of the dilated fetal urinary tract by checking for additional features (e.g., kidney and bladder length) for this period of gestation. This method is more accurate than noting the level of SERP only.

There is little research available on pediatric outcomes derived from correlations of late 2nd trimester ultrasound examination. Accurate information regarding newborn outcomes will permit mothers/families and caregivers a clearer perspective of obstetric and pediatric needs. Ours is the largest clinical series to date that pairs fetal evaluation and postnatal outcome for the late 2nd trimester. Furthermore, this was done with combined input from maternal-fetal medicine and pediatric urological specialists as an aid to forecasting outcome. This series excluded cases in which the ultrasound specified a fetal renal abnormality (e.g., ureteroceles, infantile polycystic kidney disease), because for these cases of ‘specific’ dilations, maternal counseling would be based upon an already-recognized exact diagnosis. Other series do not make such an exclusion [10]. This precision in postnatal diagnosis does not apply to cases of fetal SERP/hydronephrosis, in which postnatal outcomes are not so easily predictable. For this reason the Society for Fetal Urology (SFU) has offered a scheme to grade the ‘nonspecific’ dilatation in infants as a means to aid forecasting outcome [4]. This scheme has not been validated for fetal imaging.

Pediatric outcome monitored by measuring extent of fetal SERP has been revisited by several others (see Wilson et al. [11] for references) including ourselves [1], but there is still no clear consensus on the threshold of SERP that merits newborn follow-up [10]. It is likely that the differences in opinion are largely based on: the fact that additional ultrasound features have not been studied; the extent to which the level of dilatation may vary during the exam [12]; the fact that postnatal dilatation may ‘transition’ spontaneously to a normal pattern in infancy; and the fact that vesicoureteral reflux is present in newborns with a normal ultrasound [13].

SERP > 4 mm is significant [14], and Broadley et al. [15] showed that prognosis is related to the

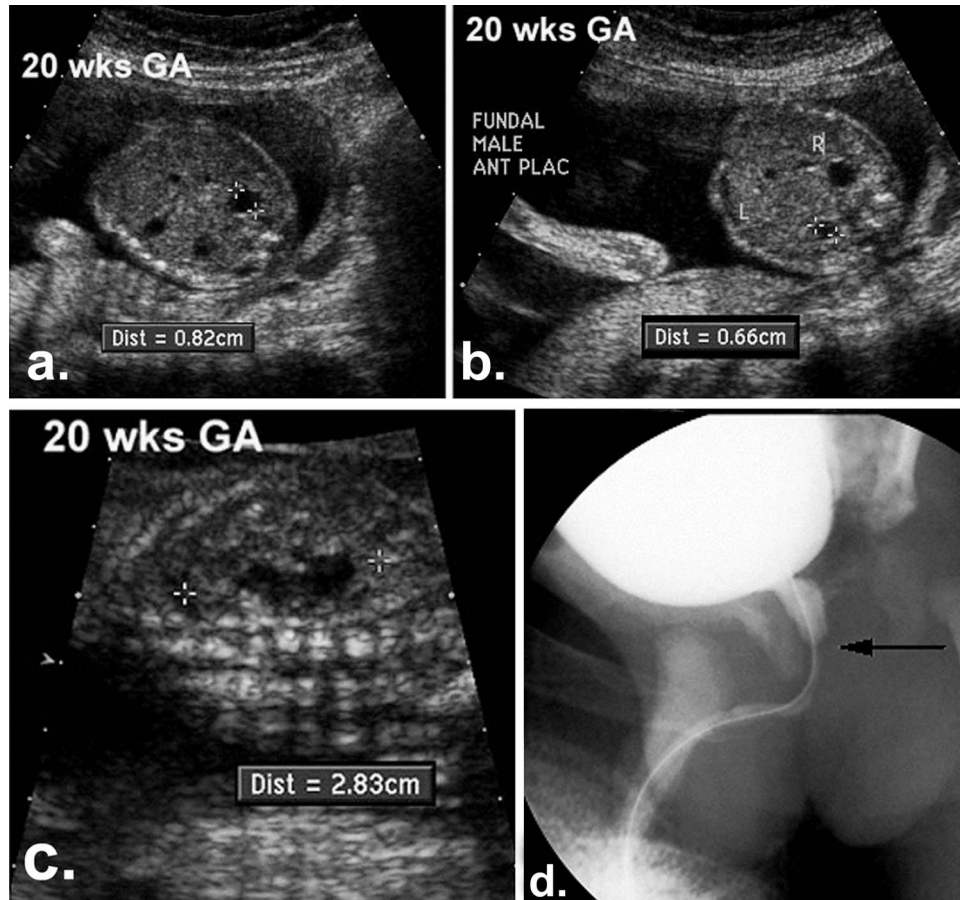


Figure 1. SERP and abnormal feature is elongated renal polar length. At 20 weeks GA transverse views of fetal ultrasound show SERP affecting (a) the left kidney at 8.2 mm and (b) the right kidney at 6.6 mm. The authors' data show that kidneys with this level of SERP that are not evaluated for additional features correspond to a 60% likelihood of extensive urological needs. The longitudinal view of the kidney (c) shows the length of the kidney is elongated at 28.3 mm (predicted upper limit of normal at 20 weeks GA is 25 mm). Because this additional feature is abnormal, there is a likelihood of extensive urological needs at 73%. (d) The newborn boy's VCUG shows the prostatic urethra is obstructed (arrow points to cutoff site between the dilated posterior urethra and membranous urethra). Cystoscopy in the newborn shows posterior urethral valves that are ablated. He has remained well without azotemia or urine infection. There is bilateral grade 2 VUR, which it is expected he will outgrow following toilet training.

degree of pelvic dilatation. Scott et al. [16] showed that the maximum dimension of the normal renal pelvis in 92.7% of fetuses was <5 mm at any gestational age. Siemens et al. [17] examined the likelihood that no postnatal follow-up was needed when the extent of SERP was: <6 mm (<20 weeks GA), <8 mm (20–30 weeks GA), and 10 mm (>30 weeks GA).

Yet, even 'minimal' SERP may show outcomes involving significant urological needs [9,12]. We confirm these observations and show that cases of SERP in which additional features were not evaluated are associated with a 52% overall incidence of extensive urological needs, involving surgery or extended urological care for various reasons (Table III). This incidence of extensive care is higher but not significantly different from that of cases of SERP in which additional features are noted as

normal (36%). However, for cases of SERP with additional feature(s) noted that are abnormal, the incidence of extensive urological needs increases significantly (89%) (Table III).

The definition of fetal hydronephrosis is not standard. Prior to about five years ago, researchers had distinguished fetal SERP from hydronephrosis only by the extent of pelvic dilatation and not by ascertaining if the dilated pelvis also shows calyceal dilatation [18–20]. More recently, there is recognition of the distinction between these two patterns, and Broadley et al. noted that fetal hydronephrosis correlates more strongly with postnatal morbidity and the need for surgery than fetal SERP [15].

We have shown that there are significant differences in level of urological care needed and performance of surgery between outcomes of fetuses that show different patterns of urinary tract dilation.

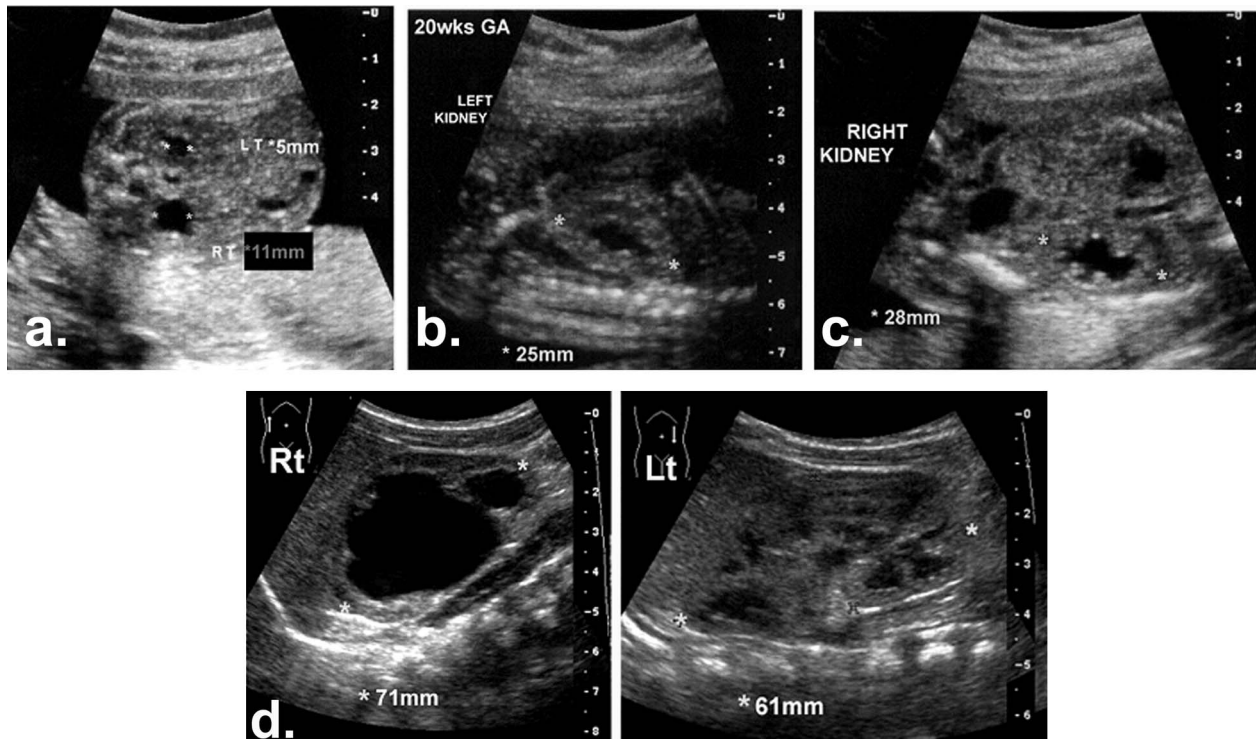


Figure 2. SERP and abnormal feature is hydronephrosis. (a) At 20 weeks there is SERP (right > left). The authors' data show that kidneys with this level of SERP (11 mm) that are not evaluated for additional features correspond to a 100% likelihood of extensive urological needs. (b) The left kidney shows normal length. (c) The right kidney shows elongated length at 28 mm (upper limit of normal is 25 mm). In this case noting the right kidney is affected by hydronephrosis does not change the likelihood prediction. (d) The newborn ultrasound shows right SFU grade 4 hydronephrosis with elongated length. This was later shown to be UPJ obstruction by WTR and pyeloplasty was subsequently done. The left kidney shows lucent medulla without hydronephrosis and is normal.

This information will improve maternal counseling regarding newborn outcome and need for surgery.

Searching for additional features in the evaluation of fetal urinary tract anomalies has been occasionally reported. Wilson et al. recognized that persistence of dilatation is important and so suggested assessing this feature by repeating the fetal sonogram during the 3rd trimester when the level of SERP was ≥ 6 mm during the 2nd trimester [11]. Liu et al. appreciated the additional feature of fetal megaureter [21]. Aviram et al. [22] showed that persistence/progression of SERP is associated with a postnatal likelihood of 'urinary tract pathology'. Montemarano et al. showed that checking for the status of bladder size in conjunction with that of the pelvic dilation is important to outcome [23]. Kleiner et al. recognized the feature of progression of hydronephrosis [24]. Bobrowski et al. [18] showed that 10% of fetuses with SERP show progression of the dilatation (≥ 3 mm), mostly in instances of bilateral fetal SERP. Broadley et al. [15] pointed out that postnatal outcome may involve morbidity if the fetal ultrasound shows additional features such as: calyceal dilatation (i.e., hydronephrosis), progression in SERP, severe hydronephrosis (SERP > 15 mm

associated with calyceal dilation), and/or visualization of a ureter. Herndon et al. related the ultrasound feature of noting an increase in renal pelvic dilation after the fetal bladder empties to the postnatal diagnosis of vesicoureteral reflux, especially if there is a family history of the condition [13].

The additional features noted likely represent the anatomic correlates of renal maldevelopment. For example, obstructed renal drainage may manifest as: elongated renal length, progression in SERP to the pattern of hydronephrosis, progression of hydronephrosis, or ureter evident. Similarly, VUR may also manifest as these features especially if there is associated bladder enlargement. Detailed assessment of these qualitative features helps assure that specific patterns of dilatation (e.g., ectopic ureter) are not confused with simple SERP/hydronephrosis patterns. An 'imaged' calyx that accompanies SERP may be distinguished from a 'dilated' calyx that accompanies hydronephrosis *in utero* as is done in babies [5]. Application of this comprehensive method to evaluate fetal renal pelvic and bladder dilation patterns permits continuity with methods to assess the newborn renal system [25], thereby allowing for more accurate expectations of postnatal care by the family.

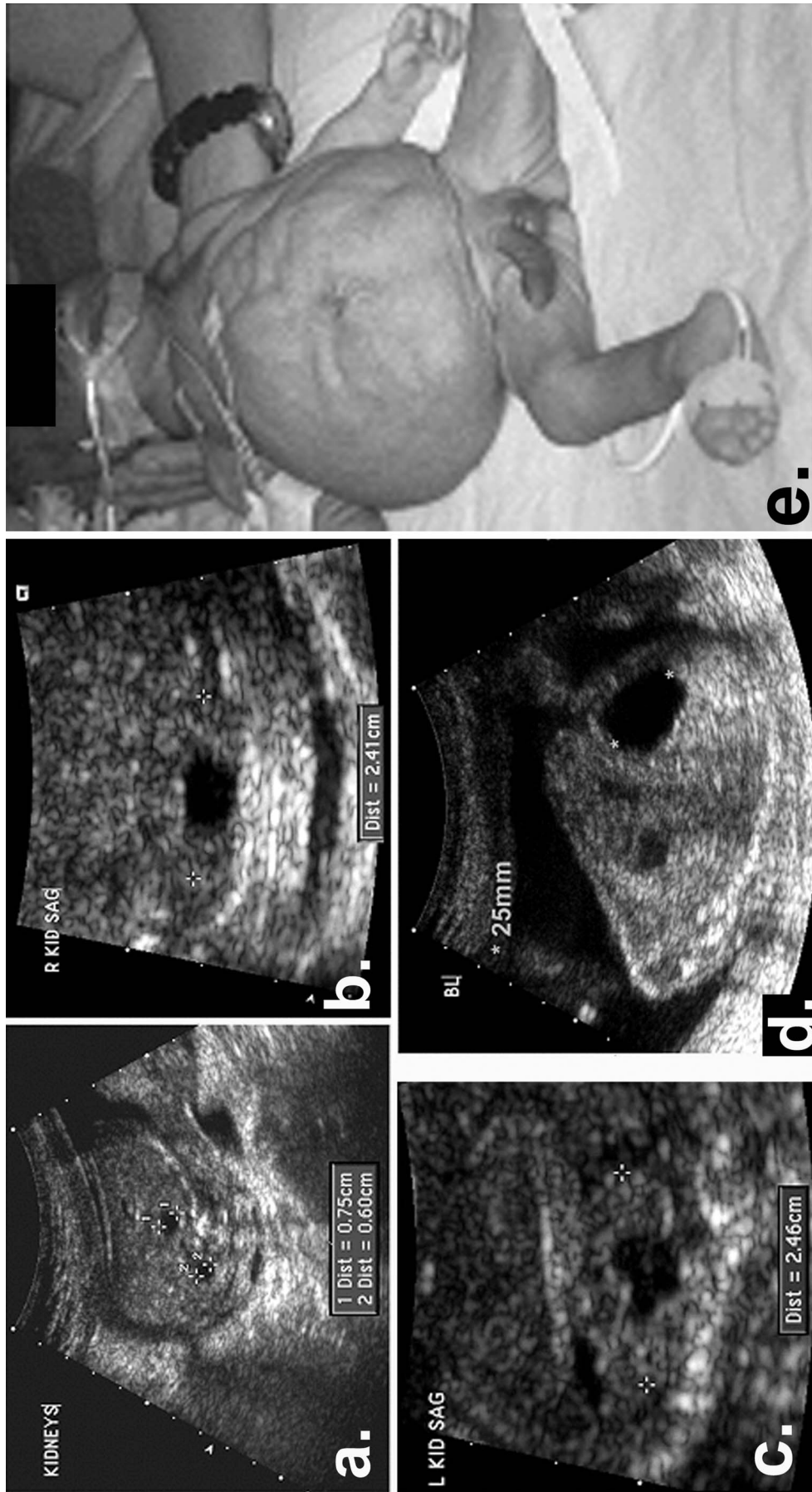


Figure 3. SERP and abnormal feature is enlarged bladder. (a) At 22 weeks there is right and left SERP, which corresponds to a 50% likelihood of extensive urological needs ((b) and(c)) The renal lengths are normal (upper limit of normal length at 22 weeks ≤ 27 mm). (d) The bladder size is enlarged (parasagittal length = 25 mm, upper limit of normal is 24 mm). Noting this additional feature corresponds to a 100% likelihood of extensive urological needs. (e) The newborn shows prune belly syndrome with bowel loops wrinkling the abdominal surface, megalourethra, and an empty scrotum because the testes are intra-abdominal.

Conclusion

Fetal kidneys between 15 and 24 weeks GA with SERP that show an abnormal additional ultrasound feature have extensive pediatric urological care significantly more often than if the features are normal or are not evaluated. As these additional features reflect renal and bladder maldevelopment, monitoring their presence permits a more comprehensive assessment of urological maldevelopment. We believe this novel method to forecast pediatric outcomes will improve maternal/parental counseling at this gestational age interval. These findings support the need for postnatal evaluation in babies with fetal SERP, especially when there is an abnormal additional ultrasound feature noted.

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