A Local Study of Maternal and Fetal Characteristics of Isolated Antenatal Hydronephrosis, and Fetal Renal Pelvis Anteroposterior Diameter in Prediction of Postnatal Urological Outcomes

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Objectives: To describe the maternal and fetal characteristics of isolated antenatal hydronephrosis (ANH), to address parental concerns by providing local data based on the fetal renal pelvis anteroposterior diameter (APD), and to determine the most effective APD cutoff in the second and third trimester for prediction of postnatal urological outcome.
Methods: A retrospective review of all cases referred to the prenatal diagnostic clinic over a 21-month period from 1 January 2013 to 30 September 2014 was performed. All the 4010 ultrasound examination reports were retrieved and those diagnostic of ANH were identified. Antenatal hydronephrosis was defined by the system based on the APD proposed by the Society for Fetal Urology. Maternal and fetal characteristics were studied. Postnatal uropathy and surgery were the events of interest.
Results: Overall, 90.8% of kidneys with isolated ANH detected in the third trimester were found to have normal anatomy after birth. Of the 153 fetuses studied, eight were identified to have postnatal uropathy of whom four underwent surgical intervention. Fetuses with second-trimester APD of >10 mm were at increased risk of postnatal uropathy (odds ratio=10.35; 95% confidence interval, 1.80-59.60; p=0.01), whereas third-trimester APD of ≥9 mm also demonstrated a significant risk (odds ratio=8.56; 95% confidence interval, 1.03-71.30; p=0.04). Third-trimester APD better predicted both postnatal uropathy and need for surgical intervention than second-trimester APD (p≤0.001). The respective best cutoff above which postnatal uropathy and surgery was anticipated were 7.3 mm and 9.6 mm in the third trimester (sensitivity 75% and specificity 76.7% for postnatal uropathy, 100% and 93.3% for surgery).
Conclusion: Fetal renal pelvis APD, particularly when measured during the third trimester, serves as a good predictor of postnatal uropathy and need for surgical intervention. Measurement of the APD remains the most important factor in predicting fetal urological outcome.
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Keywords: Hydronephrosis; Kidney pelvis; Prenatal diagnosis; Ultrasonography; Urethral obstruction

Introduction

Antenatal hydronephrosis (ANH), also known as fetal pyelectasis or dilatation of the fetal renal collecting system, is one of the most common abnormalities detected on antenatal ultrasound examination. Depending on the diagnostic criteria used to define ANH, it is reported in approximately 1% to 5% of all pregnancies[1]. ANH is twice as common in male fetuses as female[2]. It is proposed that the increased voiding pressure in male fetuses in utero causes the higher prevalence of ANH[3]. Isolated ANH has been suggested to have association with Down syndrome and most other chromosomal abnormalities[4,5], especially when additional sonographic markers are present[6]. Therefore, in fetuses with other structural abnormalities or soft markers of aneuploidy, the option of fetal karyotyping should be considered[4-7].

A variety of physiological changes in pregnancy may influence the fetal renal pelvis. ANH is 6 times more likely to occur in fetuses of mothers who themselves demonstrate hydronephrosis[7]. The relaxant effect of progesterone on the smooth muscle of the urinary tract is considered a cause for maternal hydronephrosis in pregnancy, and the same hormonal effect is likely to influence the fetal urinary tract[2]. Maternal hydration signified by maternal bladder

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fullness was found to be associated with larger fetal renal diameter by Babcook et al[8]. A study of 18 women showed that in nearly one-third of mild ANH cases, the fetal renal pelvis diameter varied according to the bladder volume, suggesting variability in the fetal renal pelvis during a bladder filling cycle[9]. Although the majority of ANH cases (41%-88%) are transient hydronephrosis with no obstructive pathology identified, ANH may signify an underlying urinary obstructive disease, such as pelvi-ureteric junction obstruction (PUJO) in 10% to 30%, vesicoureteral reflux (VUR) in 10% to 20%, or urethral obstruction or megaureters in 5% to 10% of cases[1]. Prognosis depends on a variety of factors, including the degree of ANH, amniotic fluid volume, and the presence of bilateral lesions. Evaluation and treatment of uropathy after delivery can be extensive. The diagnosis of ANH may cause significant parental anxiety[1,10].

Clinical practice varies widely regarding the evaluation of ANH fetuses. There is no uniform definition or grading for ANH in the antenatal or postnatal period. The most widely used objective parameter in current literature is the measurement of the fetal renal pelvis anteroposterior diameter (APD)[1,3,7,11,12]. Because of its simplicity, APD is favoured by 91% of maternal-fetal medicine (MFM) specialists for evaluation of ANH[13]. Several APD cutoffs above which uropathy is suspected have been considered in the literature. The majority of these vary between 4 mm and 10 mm in the second trimester and between 7 mm and 10 mm in the third trimester, with APD of >10 to 15 mm being highly suggestive of significant urinary tract pathology[3]. A grading system based on APD was published by the Society of Fetal Urology (SFU) in 2010. During the second trimester, the SFU system defines ANH as mild for APD of 4 to <7 mm, moderate for 7 to 10 mm, and severe for >10 mm. During the third trimester, mild ANH is defined as APD of 7 to <9 mm, moderate as 9 to 15 mm, and severe as >15 mm. According to a large meta-analysis, the risks of having postnatal uropathy are 11.9% for mild, 45.1% for moderate, and 88.3% for severe ANH[14].

There were three main objectives of our study. Firstly, we aimed to describe the maternal and fetal characteristics of isolated ANH cases. Secondly, we wanted to be able to address parental concerns by providing local data on the antenatal and postnatal outcomes once ANH is diagnosed, based on the SFU APD system, to compensate for the paucity of local data. Lastly, our study tried to determine the most effective APD cutoff value in the second and third trimester to predict postnatal uropathy and the need for urological surgery.

Methods

The prenatal diagnosis clinic (PDC) in the study hospital receives referrals from both the private sector and the antenatal clinic of our obstetric unit. The PDC has a well-established MFM team led by MFM subspecialist consultants with standard follow-up protocols. Once a case is referred to the PDC for ANH, detailed follow-up ultrasound scans in the second and third trimester are arranged. The maximum renal pelvis APD is measured in a transverse mid-abdominal plane showing the fetal kidneys. The fetal size, amniotic fluid index, and any other abnormalities in the fetal urinary tract are recorded. Fetuses with bilateral or unilateral APD of >7 mm in the third trimester are referred to the paediatrician for assessment in the postnatal nursery after delivery. Ultrasound of the urinary tract will be arranged by the paediatrician on postnatal day 3 to confirm the diagnosis and determine the severity of hydronephrosis, and avoid the false-negative effect due to physiological dehydration and oliguria[15,16]. The diagnoses of postnatal ultrasounds performed in the Department of Diagnostic Radiology were recorded. Additional diagnostic tests such as micturating cystourethrogram were performed according to paediatric protocols to identify postnatal uropathy. When APDs were <4 mm in the second trimester and <7 mm in the third trimester, ANH was considered resolved. The urological outcomes for these fetuses were also retrieved for review.

A retrospective review of all cases referred to the PDC over a 21-month period from 1 January 2013 to 30 September 2014 was performed. All ultrasound examination reports at the PDC during the study period were retrieved and those specifically referred for ANH were identified. All other cases, especially those referred for amniotic fluid volume and fetal urological abnormalities, were reviewed in detail and those found to have ANH were also included in the study. The SFU APD system was adopted to define ANH in the current study. Cases diagnosed to have multicystic kidney dysplasia were excluded.

Postnatal uropathy was selected as the main event of interest because the management of uropathy can be extensive, may include surgery, and causes significant anxiety to parents[10], and only conservative management is needed once normal urological anatomy is verified after delivery. The degree of worry that parents experience concerning the prognosis of uropathy is observed to be much more than that regarding conservative management in cases of normal anatomy. Fetuses referred for scan in the third trimester were studied. Maternal characteristics including age, body mass index (BMI), parity, smoking

history, history of ANH in previous pregnancies, Down syndrome screening result, as well as presence of gestational diabetes mellitus (GDM) were recorded. If Down syndrome screening showed a high risk of chromosomal abnormality, the results of confirmatory tests were retrieved. The APDs in both second and third trimester were traced in order to determine the effectiveness of APD in prediction of postnatal urological outcome. Unilateral or bilateral involvement, which kidney was involved, ANH grading, fetal sex, fetal size, and amniotic fluid volume were also studied and compared.

There is considerable variation among different studies with respect to methodology and study design. Contrary to some studies in which the larger APD was used if ANH was bilateral[11], we adopted a 'renal unit' comprising a kidney with the ipsilateral ureter down to the level of vesicoureteric junction as the basis of study, so that the clinical course of the kidneys could be better assessed, as in some other studies[7,13,17-22].

Statistical analysis was performed using the IBM Statistical Package for the Social Sciences (Windows version 22.0, SPSS Inc., Chicago [IL], US). For continuous variables, descriptive statistics were presented as mean with standard deviation. Differences in means of groups were compared using independent *t* test. Categorical variables were reported as percentages and were analysed with Pearson Chi-square test and Fisher's exact test. Multiple logistic regression was used with verification of collinearity among variables. Adjustment for confounders was carried out. Odds ratio (OR) with 95% confidence interval were calculated to determine the relationship between the APD and uropathy. Receiver operating characteristic (ROC) curves were used to assess the performance of APD in the second and third trimester in the prediction of postnatal uropathy and the need of surgical intervention. Area under the curve (AUC), sensitivity, and specificity of different APD cutoffs were calculated. Statistical significance was established for p value of <0.05.

Results

All 4010 ultrasound examination reports issued by the PDC during the 21-month study period were retrieved and studied carefully. Four fetuses were found to have multicystic kidney dysplasia and were excluded from the analysis. A total of 146 fetuses with 291 renal units were referred to the PDC for follow-up scans for ANH in the third trimester, together with another seven new referrals. The outcomes for these 153 fetuses with 305 renal units scanned are shown in Figure 1. Among these 153 fetuses, nine were lost to follow-up and hence excluded from subsequent statistical analysis. The 287 kidneys from the remaining 144 fetuses were studied. ANH was detected in 36 fetuses unilaterally and 31 fetuses bilaterally in 67 fetuses, giving rise to 98 renal units for analysis.

Although the majority of kidneys with ANH (89/98, 90.8%) were found to have normal anatomy after birth, nine (9.2%) of these 98 kidneys in eight infants exhibited postnatal uropathy. Among these eight infants, three who had unilateral ANH in the third-trimester scan were also found to have uropathy in the contralateral kidney after delivery, accounting for three (1.6%) false-negative cases in these 189 kidneys scanned normal before. Therefore, 12 kidneys in eight fetuses in total were identified to have postnatal uropathy in our study.

Comparison of maternal age, BMI, parity, smoking history, history of ANH in previous pregnancies, and presence of GDM revealed no significant differences between the two groups. All fetuses diagnosed to be high risk on Down syndrome screening underwent confirmatory tests in the current study and all were confirmed to have a normal karyotype. Down syndrome screening results did not differ much in both groups (Table 1).

Bilateral involvement and male gender did not show a significant increase in risk (OR=0.85; p=0.82 and OR=0.36; p=0.19, respectively). The APDs in the second and third trimester were studied. The distribution of kidneys with different ANH grades in both trimesters is shown in Table 1. Multivariate analysis with adjustment of confounding factors showed that fetuses with second-trimester severe ANH, i.e. APD of >10 mm, were at increased risk of postnatal uropathy (OR=10.35; p=0.01). Concerning the third-trimester ANH grading, only the moderate/severe ANH group, i.e. APD of ≥9 mm, demonstrated a significant risk of postnatal uropathy (OR=8.56; p=0.04).

Increase in APD in the second trimester did not predict postnatal uropathy well (OR=1.09; p=0.55) although such increase in the third trimester significantly increased the risk (OR=1.91; p<0.001). The ROC curves for the APD in the second and third trimester in predicting postnatal uropathy and need for surgical intervention are displayed in Figures 2 and 3. The AUC of each ROC curve was calculated. Of note, the AUC can be interpreted as the probability that a randomly selected individual from the positive group has a larger APD than whom from the negative group. The AUC for APD in the second trimester as an indicator for postnatal uropathy was 0.647 (p=0.12)

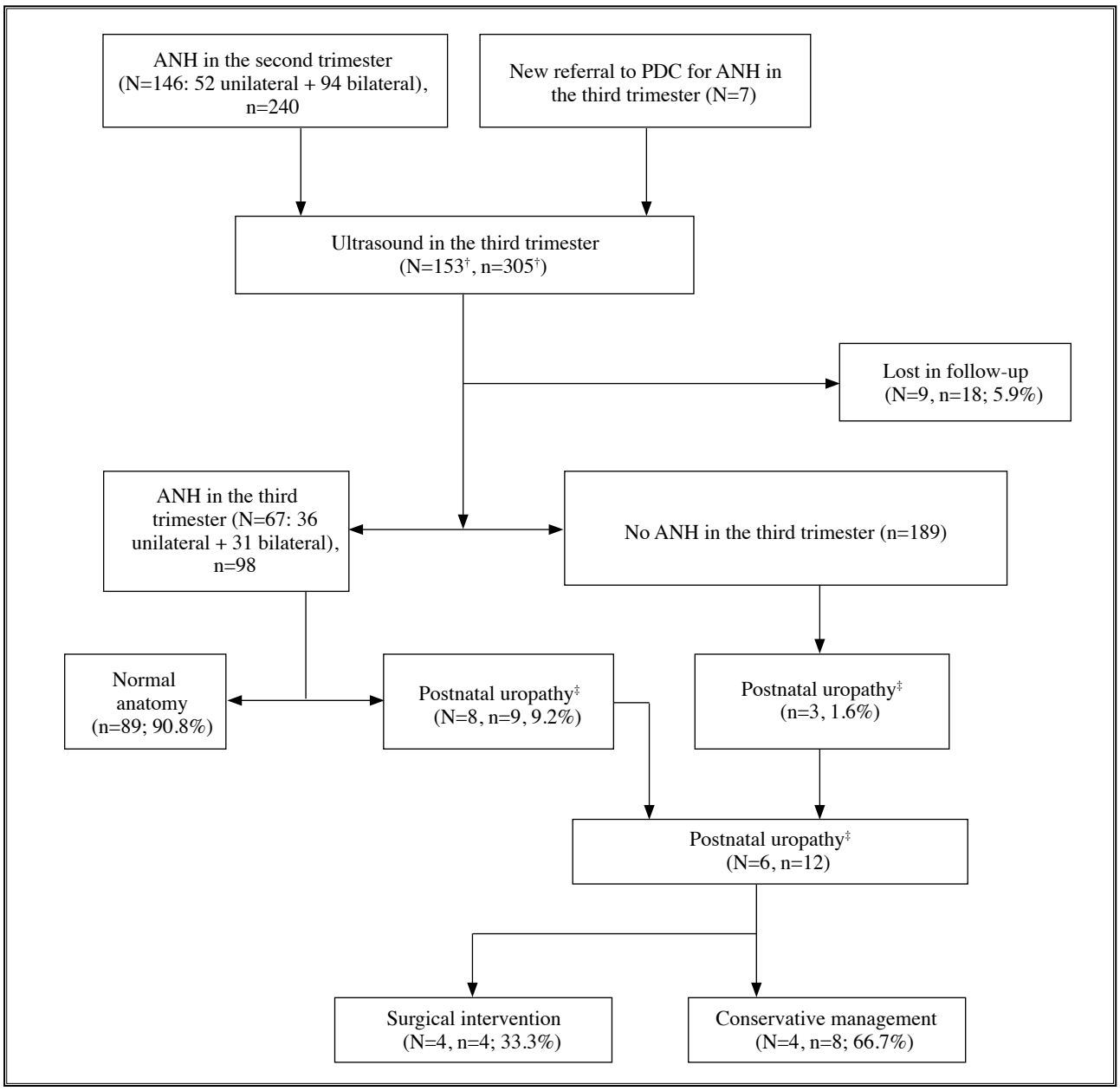

*Figure 1. Flowchart of the outcomes of fetuses and renal units**

Abbreviations: ANH = antenatal hydronephrosis; N = number of fetuses; n = number of renal units; PDC = prenatal diagnostic clinic.

* Percentages are calculated based on renal units

† One fetus had unilateral renal agenesis and ANH in the contralateral side

‡ Three kidneys with uropathy were found in the 189 renal units with no ANH in the third-trimester scan, the contralateral kidneys with ANH were detected already, giving rise to 8 fetuses with 12 pathological renal units in total (details are shown in Table 3)

while that in the third trimester was 0.843 ($p<0.001$). The AUC for APD in the second trimester as an indicator for postnatal surgery was 0.682 ($p=0.21$) while that in the third trimester was 0.986 ($p=0.001$). The third-trimester APD performed better in prediction of both postnatal uropathy and need for surgical intervention than the second trimester APD ($p\leq0.001$). The best APD cutoffs for prediction of postnatal uropathy and postnatal surgery were determined by maximising the sensitivity, i.e. true-positive rate together with specificity, i.e. true-negative rate. The best cutoffs above which postnatal uropathy and surgery can be anticipated were 6.9 mm and 10 mm respectively in the second trimester, and 7.3 mm and 9.6 mm respectively in the third trimester. The sensitivity and specificity of

Table 1. Comparison of maternal and fetal characteristics of third-trimester ANH cases with postnatal uropathy*

	Normal anatomy (n=89)	Uropathy identified (n=9)	p Value	Odd ratio (95% confidence interval)	p Value
Maternal age at booking visit (years)	30.29 ± 4.30	30.33 ± 5.61	0.98	1.01 (0.83-1.23)	0.91
BMI at booking visit (kg/m^2)	22.39 ± 3.30	21.26 ± 2.45	0.33	0.97 (0.72-1.30)	0.82
Parity			0.49	0.32 (0.05-2.04)	0.23
0	37 (42)	5 (56)			
≥1	52 (58)	4 (44)			
Smoking history			1.00	-	-
Non-smoker	83 (93)	9 (100)			
Ex-smoker / current smoker	6 (7)	0			
History of ANH in previous pregnancy			1.00	-	-
No	85 (96)	9 (100)			
Yes	4 (4)	0			
NT (MoM)	1.02 ± 0.26	0.84 ± 0.42	0.26	0.23 (0.02-2.92)	0.26
AFP (MoM)	1.13 ± 0.21	0.69 ± 0.00	0.16	0.00 (0.00-0.01)	0.99
bHCG (MoM)	1.13 ± 0.61	5.76 ± 10.94	0.001	1.96 (0.83-4.63)	0.13
PAPP-A (MoM)	0.97 ± 0.49	1.41 ± 1.93	0.16	1.71 (0.75-3.92)	0.20
Down syndrome screening result			0.31	5.38 (0.32-89.41)	0.24
Low risk	71 (80)	6 (67)			
High risk	3 (3)	1 (11)			
Not done	15 (17)	2 (22)			
GDM			0.05	1.66 (0.25-11.00)	0.60
Yes	76 (85)	5 (56)			
No	13 (15)	4 (44)			
Gestational age at scan (days)	241.81 ± 10.74	251.56 ± 9.55	0.01	1.15 (1.06-1.24)	0.001
Laterality in third trimester			0.82	0.85 (0.21-3.34)	0.82
Bilateral	53 (60)	5 (56)			
Unilateral	36 (40)	4 (44)			
Kidney side			0.73	1.66 (0.41-6.78)	0.48
Left	49 (55)	4 (44)			
Right	40 (45)	5 (56)			
APD in second trimester (mm)	6.58 ± 2.20	7.10 ± 3.89	0.56	1.09 (0.81-1.47)	0.55
ANH grading in second trimester					
Normal	1 (1)	1 (11)	0.12	1.00†	†
Mild	45 (51)	2 (22)	0.07	0.26 (0.05-1.42)	0.12
Moderate	24 (27)	2 (22)	1.00	0.83 (0.15-4.61)	0.84
Severe	5 (6)	3 (33)	0.03	10.35 (1.80-59.60)	0.01
Missing APD	14 (16)	1 (11)	-	-	-

Abbreviations: AFP = alpha fetoprotein; AGA = appropriate for gestational age; ANH = antenatal hydronephrosis; APD = anteroposterior diameter; bHCG = beta human chorionic gonadotropin; BMI = body mass index; GDM = gestational diabetes mellitus; LGA = large for gestational age; MoM = multiple of median; NT = nuchal translucency; PAPP-A = pregnancy-associated plasma protein A; SGA = small for gestational age

* Data are shown as mean ± standard deviation or No. (%)

† Fetuses with normal APD were selected as the reference group

‡ Moderate and severe ANH groups were combined because of presence of zero cell count

Table 1. (cont'd)

	Normal anatomy (n=89)	Uropathy identified (n=9)	p Value	Odd ratio (95% confidence interval)	p Value
APD in third trimester (mm)	8.73 ± 1.67	13.22 ± 3.49	0.000	1.91 (1.38-2.65)	0.000
ANH grading in third trimester					
Mild	46 (52)	1 (11)	0.03	0.12 (0.01-0.97)	0.05
Moderate	43 (48)	5 (56)	0.74	8.56 (1.03-71.30)‡	0.04‡
Severe	0	3 (33)	0.001	‡	‡
Fetal sex			0.37	0.36 (0.08-1.67)	0.19
Male	73 (82)	6 (67)			
Female	16 (18)	3 (33)			
Fetal size			0.59		
AGA	78 (88)	9 (100)		-	-
SGA	0	0		-	-
LGA	11 (12)	0		-	-
Liquor volume			1.00		
Normal	87 (98)	9 (100)		-	-
Decreased	0	0		-	-
Increased	2 (2)	0		-	-

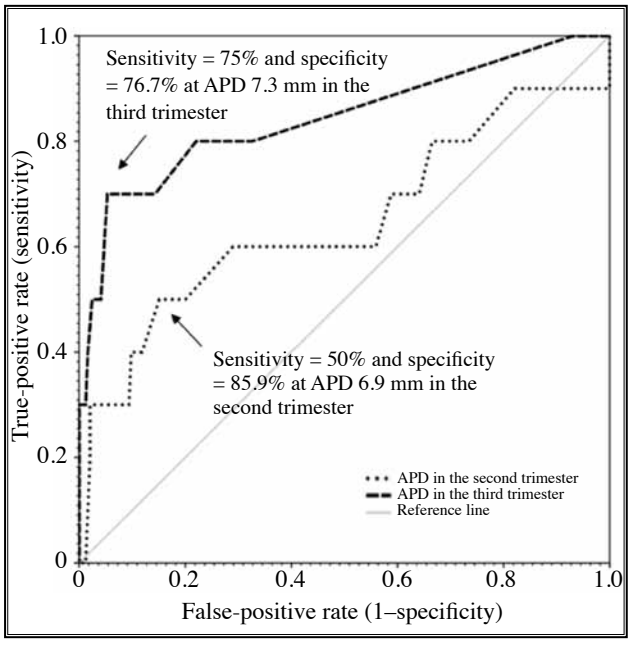

Figure 2. Renal pelvis anteroposterior diameter (APD) to predict postnatal uropathy

Area under the curve for APD in the second trimester was 0.647 (95% confidence interval, 0.430-0.863, p=0.12), and that in the third trimester was 0.843 (95% confidence interval, 0.685-1.000, p<0.001)

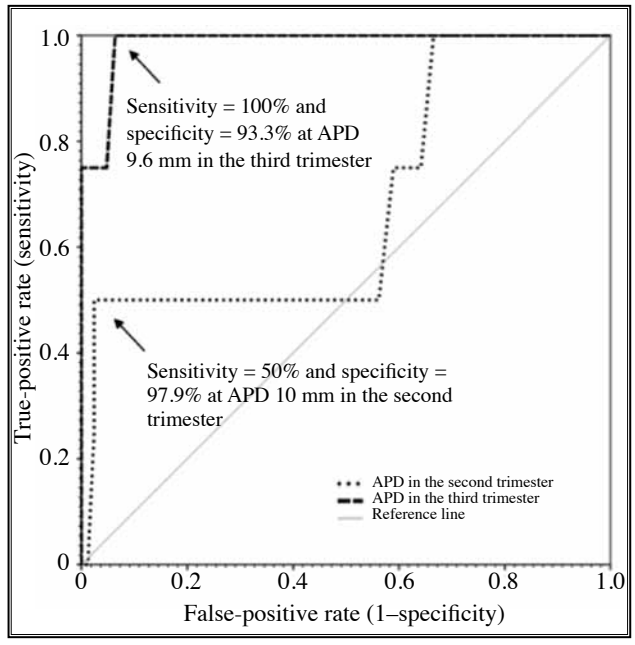

Figure 3. Renal pelvis anteroposterior diameter (APD) to predict postnatal surgical intervention

Area under the curve for APD in the second trimester was 0.682 (95% confidence interval, 0.388-0.977, p=0.21), and that in the third trimester was 0.986 (95% confidence interval, 0.961-1.000, p=0.001)

different APD cutoffs are shown in Table 2 and Figures 2 and 3.

Discussion

The current definition of ANH is variable and management shows diversity among different centres. There is little agreement on the best protocol for follow-up. Over decades different diagnostic systems have been proposed to establish a threshold value to distinguish normal fetal renal pelvis dilatation from pathological cases. The SFU proposed a five-grade system in 1993 based on the ultrasound appearance of the renal parenchyma and pelvicalyceal system[1]. This SFU system has been shown to have good intra-rater, but fair inter-rater reliability[23]. While Zhan et al[24] used an ultrasound scoring system comprising renal pelvic dilatation together with parenchymal thickness and pelvicalyceal morphology for 158 Chinese fetuses, Leung et al[25] from a local tertiary centre advocated a different fetal hydronephrosis index with incorporation of the volume of fetal urinary bladder, so eliminating the confounding effect of a full bladder. Both showed promising results. Recently in mid-2014, a multidisciplinary panel produced a consensus on the classification of prenatal and postnatal urinary tract dilatation in order to promote effective and accurate communication between different specialists[26]. Apart from the SFU definition of ANH based on APD, additional sonographic features of fetal renal parenchyma, bladder and ureters were included in the risk stratification. Extensive evaluation will be required to assess its effectiveness in predicting fetal outcome in the future. To date, APD remains the most widely used parameter in the management of ANH. Corteville et al[27] recommended an APD of >4 mm before 33 weeks of gestation, and >7 mm after 33 weeks of gestation to warrant postnatal follow-up. Some authors proposed that the risk of significant postnatal uropathy would be minimal if APD was <10 mm in the third trimester[17], whereas Gotoh et al[28] suggested that surgery would not be necessary if APD was <20 mm between 30 and 40 weeks of gestation.

The diagnosis of ANH causes significant parental anxiety and obstetrician's uncertainty in management. Counselling of parents is often based on the obstetrician's personal knowledge and belief[1,10,18]. Our data showed that the vast majority of ANH cases in the third trimester turned out to have normal urological anatomy (89/98, 90.8%).

Table 2. Efficacy of different renal pelvis APDs in predicting postnatal urological outcomes*

APD (mm)	Prediction of postnatal uropathy				Prediction of postnatal surgery			
	Second trimester		Third trimester		Second trimester		Third trimester	
	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
≥3	92.9	16.1	1.00	1.5	100	16.4	100	1.3
≥4	85.7	29.3	1.00	4.1	100	30.6	100	4.0
≥5	64.3	61.8	1.00	7.8	50.0	61.2	100	7.3
≥6	50.0	81.1	75.0	66.7	50.0	80.4	100	65.7
≥7	42.9	89.2	75.0	76.3	50.0	88.6	100	75.3
≥8	35.7	93.6	56.3	83.7	50.0	93.2	100	83.7
≥9	28.6	96.4	56.3	94.1	50.0	96.1	100	93.0
≥10	21.4	98.0	37.5	95.6	50.0	97.9	75.0	95.0
≥11	0.00	98.8	37.5	97.4	0.00	98.9	75.0	96.7
≥12	0.00	99.2	31.3	98.5	0.00	99.3	75.0	98.0
≥13	0.00	100	25.0	98.9	0.00	100	75.0	98.7
≥14	NA	NA	25.0	100	NA	NA	75.0	99.7
≥15	NA	NA	18.8	100	NA	NA	50.0	99.7
≥16	NA	NA	12.5	100	NA	NA	50.0	100
≥17	NA	NA	6.3	100	NA	NA	25.0	100
≥18	NA	NA	0.00	100	NA	NA	0.00	100

Abbreviations: APD = anteroposterior diameter; TPR = true-positive rate; TNR = true-negative rate; NA = not available

* Data are shown as TPR (sensitivity) or TNR (specificity) in percentages

Compliance with postnatal follow-up is all that is needed for these cases.

Although the left kidney has been shown to be more likely to develop ANH[29], our study did not confirm a prevalence of ANH and uropathy in the left kidney, and side of kidney involvement was unrelated to clinical outcome (OR=1.66; p=0.48). Male fetuses are more likely to be affected by ANH, in accordance with a male predominance of various postnatal uropathies[3,30,31]. Bilateral hydronephrosis is of greater concern particularly in a male fetus with abnormal amniotic fluid volume[32,33]. Both bilateral involvement and male gender were not shown to have a significant risk for developing uropathy in the current study (OR=0.85; p=0.82 and OR=0.36; p=0.19 respectively). One reason might be the relatively small incidence of the outcome of interest, i.e. postnatal uropathy in our study.

Studies that have quantified the risk of postnatal uropathy for different ANH grades are limited, especially when APD is used for grading severity of ANH. Lee et al[14] summarised the risk of postnatal uropathy as 11.9% for mild, 45.1% for moderate, and 88.3% for severe ANH. ORs were used in the current study to express risk of adverse fetal urological outcome. When only second-trimester APD was considered, severe ANH, i.e. APD of >10 mm, had an upsurge in postnatal uropathy (OR=10.35; p=0.01). There was a more than 8-fold increase in the risk of postnatal uropathy for the moderate/severe ANH group in the third trimester when APD was ≥9 mm (OR=8.56; p=0.04). These findings support the suggestion according to the review issued by a multidisciplinary panel that moderate and severe ANH warrant an ultrasound evaluation to determine progression of urinary tract dilatation[26]. These data are beneficial in providing information to facilitate prenatal counselling.

The statistical significance of high AUC for third-trimester APD (Figures 2 and 3) shows that APD in the third trimester is useful to predict both postnatal uropathy and need for surgical intervention. It was consistent with the comment by Bouzada et al[12] that APD after 28 weeks of gestation is a simple and efficient tool to screen for possible significant uropathy and the AUC quoted was 0.900. The best APD cutoff for prediction of postnatal uropathy in our study was 7.3 mm in the third trimester, when we tried to maximise the sensitivity but not deprive the specificity much, hence giving a higher true-positive rate and a lower false-negative rate. These findings are comparable with those of Corteville et al[27] who recommended a cutoff at 7 mm in the third trimester. A systematic review by Ismaili et al[34] also proposed the cutoff at 7 mm. The recommendation by Corteville et al[27] was criticised for the high false-positive rate, APD ≥4 mm prior to 33 weeks of gestation and ≥7 mm after 33 weeks showed a sensitivity of 100% and false-positive rates of 30% to 80%[3], similar to the finding of Bouzada et al[12] that the sensitivity and specificity for the best cutoff at 7.5 mm was 97.9% and 40.6%, respectively. On the contrary, the third-trimester APD of 7.3 mm from our analysis achieved a balance between sensitivity and specificity in predicting postnatal uropathy and need for surgery (sensitivity 75% and specificity 76.7%). The sensitivity and specificity of the APD at 7 mm as the best cutoff in a study of similar sample size to ours was 87% and 85%, respectively[35].

Different cutoff values are chosen in different centres, depending on the sensitivity and specificity required. The best cutoff for need for surgical intervention is more variable among different studies, ranging mostly from 10 mm to 15 mm[7,11,12,20,36], possibly because the need for postnatal surgery may be influenced by a variety of factors such as pathology, postnatal renal function, difference in the surgeon's practice, and parental preference. The APD cutoff for prediction of the need for postnatal surgery at 9.6 mm in our study showed high sensitivity of 100% and specificity of 93.3%. In view of the good predictive value of third-trimester APD as shown by various studies and our analysis, an institute may consider delaying the follow-up scan to the third trimester when a fetus is referred for ANH at an earlier gestation, especially when ANH is mild. The reduced frequency of investigations decreases parental anxiety[10], and perhaps also allows better allocation of manpower and resources in a busy PDC. Further research will help to verify the best time of evaluation for ANH cases.

Eight infants with 12 renal units were found to have postnatal uropathology in our study (Table 3). Consistent with the prevalence in the current literature, PUJO and VUR remained the most common pathologies. Postnatal uropathy was chosen as the major outcome of interest in our analysis as the need to undergo surgical intervention may be influenced by a variety of factors. In addition, most postnatal uropathy can be detected in early infancy. Other limitations of our study include those common to most other retrospective studies. The retrospective nature of data collection may lead to incompleteness of data for analysis. Larger-scale study and longer follow-up are preferable. Postnatal events such as urinary tract infection[37-39] take time to develop, and the need for surgical intervention may

Table 3. Summary of the eight infants with postnatal uropathy

Case No.	Sex	Renal pelvis anteroposterior diameter (mm)				Postnatal uropathy (12 renal units)	Management
		Second trimester		Third trimester			
		Left	Right	Left	Right		
1	Male	4	3	6*	12†	Bilateral grade 5 VURs	Conservative
2	Male	NA	NA	6*	16†	Left grade 2 VUR Right grade 3 VUR	Conservative
3	Male	9.1	10.6	9	14†	Right PUJO	Right pyeloplasty
4	Male	4.8	8.1	17†	6	Left distal ureteric stricture	Resection of stricture
5	Female	10	7.9	11†	8†	Left grade 4 VUR Right grade 3 VUR	Conservative
6	Male	11	5.8	15†	8	Left PUJO	Left pyeloplasty
7	Male	6	11	6*	13†	Bilateral ureteroceles	Conservative
8	Female	4.5	4.8	10†	10	Left megaureter	Insertion of J-J stent

Abbreviations: NA = not available; PUJO = pelvi-ureteric junction obstruction; VUR = vesicoureteric reflux

* Three false-negative cases in the 189 renal units with no antenatal hydronephrosis identified in the third-trimester scan

† Nine true-positive cases in the 98 renal units with antenatal hydronephrosis identified in the third-trimester scan

evolve in later infancy, thus longer observation might be needed. The subjective nature of antenatal and postnatal ultrasound examinations may be a confounder. Data on features of renal parenchyma, calyces and ureters were not consistently obtained, and they might reflect more severe obstructive uropathy.

The strength of our study is that all fetuses were followed up in a single antenatal ultrasound unit with good standard and consistency in definition and care of ANH throughout. We had a low proportion of cases lost to follow-up compared with some other studies (Figure 1). Lee et al[14] reported in a meta-analysis that 246 (15%) of 1678 patients with ANH were lost to follow-up. Last but not least, our study helps in the provision of local data on ANH. We hope the results of this analysis will be useful in our prenatal counselling and relief of parental anxiety.

In conclusion, fetal renal pelvis APD, particularly when measured in the third trimester, serves as a good predictor of postnatal uropathy and need for surgical intervention. Anteroposterior diameter measurement remains the most important factor in predicting fetal urological outcome. The best APD cutoff in the prediction of postnatal urological outcome depends on the choice of sensitivity and specificity of the test.

References

1. Nguyen HT, Herndon CD, Cooper C, et al. The Society for Fetal Urology consensus statement on the evaluation and management of antenatal hydronephrosis. *J Pediatr Urol* 2010; 6:212-31.
2. Adra AM, Mejides AA, Dennaoui MS, Beydoun SN. Fetal pyelectasis: is it always "physiologic"? *Am J Obstet Gynecol* 1995; 173:1263-6.
3. Toiviainen-Salo S, Garel L, Grignon A, et al. Fetal hydronephrosis: is there hope for consensus? *Pediatr Radiol* 2004; 34:519-29.
4. Wickstrom EA, Thangavelu M, Parilla BV, Tamura RK, Sabbagha RE. A prospective study of the association between isolated fetal pyelectasis and chromosomal abnormality. *Obstet Gynecol* 1996; 88:379-82.
5. Benacerraf BR, Mandell J, Estroff JA, Harlow BL, Frigoletto FD Jr. Fetal pyelectasis: a possible association with Down syndrome. *Obstet Gynecol* 1990; 76:58-60.
6. Bornstein E, Barnhard Y, Donnenfeld AE, Ferber A, Divon MY. The risk of a major trisomy in fetuses with pyelectasis: the impact of an abnormal maternal serum screen or additional sonographic markers. *Am J Obstet Gynecol* 2007; 196:e24-6.
7. Gramellini D, Fieni S, Caforio E, et al. Diagnostic accuracy of fetal renal pelvis anteroposterior diameter as a predictor of significant postnatal nephrouropathy: second versus third

trimester of pregnancy. *Am J Obstet Gynecol* 2006; 194:167-73.
8. Babcook CJ, Silvera M, Drake C, Levine D. Effect of maternal hydration on mild fetal pyelectasis. *J Ultrasound Med* 1998; 17:539-44.
9. Damen-Elias HA, Stigter RH, De Jong TP, Visser GH. Variability in dilatation of the fetal renal pelvis during a bladder filling cycle. *Ultrasound Obstet Gynecol* 2004; 24:750-5.
10. Harding LJ, Malone PS, Wellesley DG. Antenatal minimal hydronephrosis: is its follow-up an unnecessary cause of concern? *Prenat Diagn* 1999; 19:701-5.
11. Shamshirsaz AA, Ravangard SF, Egan JF, et al. Fetal hydronephrosis as a predictor of neonatal urologic outcomes. *J Ultrasound Med* 2012; 31:947-54.
12. Bouzada MC, Oliveira EA, Pereira AK, et al. Diagnostic accuracy of fetal renal pelvis anteroposterior diameter as a predictor of uropathy: a prospective study. *Ultrasound Obstet Gynecol* 2004; 24:745-9.
13. Zanetta VC, Rosman BM, Bromley B, et al. Variations in management of mild prenatal hydronephrosis among maternal-fetal medicine obstetricians, and pediatric urologists and radiologists. *J Urol* 2012; 188:1935-9.
14. Lee RS, Cendron M, Kinnamon DD, Nguyen HT. Antenatal hydronephrosis as a predictor of postnatal outcome: a meta-analysis. *Pediatrics* 2006; 118:586-93.
15. Mouriquand PD, Troisfontaines E, Wilcox DT. Antenatal and perinatal uro-nephrology: current questions and dilemmas. *Pediatr Nephrol* 1999; 13:938-44.
16. Elder JS. Antenatal hydronephrosis. Fetal and neonatal management. *Pediatr Clin North Am* 1997; 44:1299-321.
17. Duin LK, Willekes C, Koster-Kamphuis L, Offermans J, Nijhuis JG. Fetal hydronephrosis: does adding an extra parameter improve detection of neonatal uropathies? *J Matern Fetal Neonatal Med* 2012; 25:920-3.
18. Wollenberg A, Neuhaus TJ, Willi UV, Wisser J. Outcome of fetal renal pelvic dilatation diagnosed during the third trimester. *Ultrasound Obstet Gynecol* 2005; 25:483-8.
19. Longpre M, Nguan A, Macneily AE, Afshar K. Prediction of the outcome of antenatally diagnosed hydronephrosis: a multivariable analysis. *J Pediatr Urol* 2012; 8:135-9.
20. Kim HJ, Jung HJ, Lee HY, et al. Diagnostic value of anteroposterior diameter of fetal renal pelvis during second and third trimesters in predicting postnatal surgery among Korean population: useful information for antenatal counseling. *Urology* 2012 ;79:1132-7.
21. Thornburg LL, Pressman EK, Chelamkuri S, Hulbert W, Rabinowitz R, Mevorach R. Third trimester ultrasound of fetal pyelectasis: predictor for postnatal surgery. *J Pediatr Urol* 2008; 4:51-4.
22. Passerotti CC, Kalish LA, Chow J, et al. The predictive value of the first postnatal ultrasound in children with antenatal hydronephrosis. *J Pediatr Urol* 2011; 7:128-36.
23. Keays MA, Guerra LA, Mihill J, et al. Reliability assessment of Society for Fetal Urology ultrasound grading system for hydronephrosis. *J Urol* 2008; 180(4 Suppl):1680-3.
24. Zhan X, Tao G, Cheng L, Liu F, Li H, Liu S. Ultrasound score: a new method to differentiate fetal physiological and pathological hydronephrosis. *Eur J Obstet Gynecol Reprod Biol* 2010; 151:26-32.
25. Leung VY, Chu WC, Metreweli C. Hydronephrosis index: a better physiological reference in antenatal ultrasound for assessment of fetal hydronephrosis. *J Pediatr* 2009; 154:116-20.
26. Nguyen HT, Benson CB, Bromley B, et al. Multidisciplinary consensus on the classification of prenatal and postnatal urinary tract dilation (UTD classification system). *J Pediatr Urol* 2014; 10:982-98.
27. Corteville JE, Gray DL, Crane JP. Congenital hydronephrosis: correlation of fetal ultrasonographic findings with infant outcome. *Am J Obstet Gynecol* 1991; 165:384-8.
28. Gotoh H, Masuzaki H, Fukuda H, Yoshimura S, Ishimaru T. Detection and assessment of pyelectasis in the fetus: relationship to postnatal renal function. *Obstet Gynecol* 1998; 92:226-31.
29. van Eerde AM, Meutgeert MH, de Jong TP, Giltay JC. Vesico-ureteral reflux in children with prenatally detected hydronephrosis: a systematic review. *Ultrasound Obstet Gynecol* 2007; 29:463-9.
30. Leung VY, Chu WC, Metreweli C. Prenatal ultrasound study of gender difference in urinary tract morphology in normal fetuses. *HK J Paediatr (New Series)* 2008; 13:165-70.
31. Cohen-Overbeek TE, Wijngaard-Boom P, Ursem NT, Hop WC, Wladimiroff JW, Wolffenbuttel KP. Mild renal pyelectasis in the second trimester: determination of cut-off levels for postnatal referral. *Ultrasound Obstet Gynecol* 2005; 25:378-83.
32. Fefer S, Ellsworth P. Prenatal hydronephrosis. *Pediatr Clin North Am* 2006; 53:429-47.
33. Yiee J, Wilcox D. Management of fetal hydronephrosis. *Pediatr Nephrol* 2008; 23:347-53.
34. Ismaili K, Hall M, Piepsz A, Alexander M, Schulman C, Avni FE. Insights into the pathogenesis and natural history of fetuses with renal pelvis dilatation. *Eur Urol* 2005; 48:207-14.
35. Odibo AO, Raab E, Elovitz M, Merrill JD, Macones GA. Prenatal mild pyelectasis: evaluating the thresholds of renal pelvic diameter associated with normal postnatal renal function. *J Ultrasound Med* 2004; 23:513-7.
36. de Kort EH, Bambang Oetomo S, Zegers SH. The long-term outcome of antenatal hydronephrosis up to 15 millimetres justifies a noninvasive postnatal follow-up. *Acta Paediatr* 2008; 97:708-13.
37. Lee JH, Choi HS, Kim JK, et al. Nonrefluxing neonatal hydronephrosis and the risk of urinary tract infection. *J Urol* 2008; 179:1524-8.
38. Sencan A, Carvas F, Hekimoglu IC, et al. Urinary tract infection and vesicoureteral reflux in children with mild antenatal hydronephrosis. *J Pediatr Urol* 2014; 10:1008-13.
39. Walsh TJ, Hsieh S, Grady R, Mueller BA. Antenatal hydronephrosis and the risk of pyelonephritis hospitalization during the first year of life. *Urology* 2007; 69:970-4.