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ORIGINAL ARTICLE

Foetal Hydronephrosis and Urinary Tract Anomalies: Third Trimester Versus 20-week Scan

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Abstract:
Background and Aims: Foetal hydronephrosis may be associated with urinary tract disease and therefore a 20-week anomaly scan is recommended during pregnancy. Some reports have shown that ultrasound scanning later in pregnancy may also detect foetal hydronephrosis. In this study, we compare the incidence of urinary tract anomalies diagnosed following foetal hydronephrosis detected incidentally in late pregnancy versus at the recommended 20-week ultrasound scan.
Material and Methods: A routine 20-week anomaly scan was performed on 4992 pregnant women, and if foetal hydronephrosis was present, a scan was repeated at 28 weeks. Persistence of hydronephrosis at 28 weeks defined Group A. Group B consisted of hydronephrotic foetuses discovered on incidental third trimester scan. The incidence of urinary tract anomalies detected postnatally was compared.
Results: The findings in group A (n=44 infants) included: vesico-ureteric reflux (VUR) (1), pelvi-ureteric junction obstruction (1). In group B (12 infants, of whom 8 had an earlier normal 20-week scan) the findings included: VUR (2), multicystic dysplastic kidney (1), posterior urethral valve (1). The relative risk for VUR was 16.16 times higher (95% CI 0.80- 953.9) with hydronephrosis diagnosed in the 3rd trimester.
Conclusion: The rate of urinary tract anomalies diagnosed after hydronephrosis on third trimester ultrasound scan is therefore higher than the recommended 20-week anomaly scan which may be falsely reassuring.

Keywords: Pregnancy; ultrasonography; kidney; hydronephrosis; abnormalities
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Introduction

Foetal hydronephrosis is usually diagnosed at the antenatal 20-week anomaly scan which is recommended as a minimum standard during pregnancy [1]. It may be associated with urinary tract disease secondary to vesico-ureteric reflux (VUR), anatomical obstruction and multicystic dysplastic kidney (MCDK) [2, 3]. Although most cases of antenatal hydronephrosis are temporary and resolve on subsequent antenatal or post-natal scans, those that persist necessitate post-natal antibiotic prophylaxis and further uroradiological investigations [2, 4-7]. This approach is justified by the increased risk of urinary tract infection (UTI) associated with an underlying VUR [8]. However mild hydronephrosis is less often

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associated with underlying significant pathology and may not always require postnatal investigations [3, 9]. On the other hand, foetal assessment and intervention may be required in some cases [10].

Some reports have shown that ultrasound scanning later in pregnancy may also detect foetal hydronephrosis associated with urinary tract anomalies, with more marked hydronephrosis associated with more significant pathology [11-14]. However no formal comparison between the value of such late scans and the recommended 20-week anomaly scan has been reported before.

We therefore compare the rate of postnatally diagnosed urinary tract anomalies when hydronephrosis was diagnosed incidentally in late pregnancy versus the recommended routine 20-week anomaly scan.

Material and Methods

This was a retrospective descriptive observational study of a cohort of 4992 pregnant women between January 2006 and December 2007. They underwent a routine anomaly antenatal scan between 18 and 21 weeks, undertaken by a group of 4 fully trained and accredited sonographers, using a General Electric LOGIQ 400 CL ultrasound scanner (3.5 MHz Wideband convex transducer, software version 3.41, GE Healthcare, Global Headquarters, Pollards Wood, Nightingales Lane, Chalfont St Giles, BUCKS, HP8 4SP, United Kingdom).

The maximum antero-posterior pelvic diameter (APPD) of the foetal kidneys was measured in the transverse plane, in addition to the detection of other congenital anomalies [1]. Antenatal hydronephrosis was defined when APPD was >5mm. Four grades of dilatation were defined: APPD: equal or greater than 5 and under 10 mm, equal or greater than 10 and under15 mm, equal or greater than 15 and under 20 mm and equal or greater than 20 mm. The presence of calyceal dilalation, oligohydramnios and a distended bladder was also noted during this scan. For the purpose of this study, all foetuses with aneuploidy and/or multiple congenital anomalies outside the urinary tracts were excluded from analysis. All cases with hydronephrosis were rescanned at 28 weeks of gestation, those with persistent dilatation (>5 mm) constituted group A and required postnatal imaging. Those without residual dilatation at 28 weeks did not undergo postnatal imaging as per our department guidelines.

In the same population of 4492 pregnant women, foetal hydronephrosis diagnosed by the same sonographers on incidental third trimester findings (carried out mainly for obstetrical reasons) were included in the study (as group B) when APPD was > 5mm.

After birth, infants from both groups A and B were managed according to a well defined protocol. Trimethoprim® prophylaxis was started at birth and a postnatal ultrasound was carried out between day 5 and day 10. Other imaging studies were performed only if dilatation persisted on postnatal ultrasound. These included a micturating cystourethrogram (MCUG) in males or 99m Tc-labelled mercapto-acetyl triglycine (MAG 3) direct nuclear cystogram in females to diagnose VUR, which was graded I to V according to the international classification. The choice of MCUG for boys and not girls was that it offers a better anatomical visualisation of the posterior urethra to exclude valves. A 99m Tc-labelled dimercaptosuccinic acid (DMSA) scintigraphy was performed in infants diagnosed to have VUR or multicystic dysplastic kidney (MCDK), in order to diagnose areas of poorly functioning parenchyma and also to assess differential renal function. In the absence of VUR a 99m Tc-labelled mercapto-acetyl triglycine (MAG 3) renogram with diuretic was carried out to investigate the possibility of obstruction, which was defined by delayed excretion of the isotope persisting after diuretic administration. In the absence of VUR and obstruction, persistent hydronephrosis was defined as idiopathic dilatation and children were followed up with serial ultrasound scans. All infants were followed up for between 9 and 24 months. The outcomes of interest were the urinary tract anomalies diagnosed by those imaging studies which were carried out in the postnatal period. They included VUR, anatomical urinary tract obstruction (posterior urethral valve or PUV and pelvi-ureteric junction obstruction or PUJO) and MCDK. As the primary purpose was the detection of anomalies associated with antenatal hydronephrosis incidentally discovered on the third trimester scan compared to the 20-week scan, we deliberately omitted from the third trimester hydronephrotic group the foetuses

who were already known to have hydronephrosis on earlier scans.

The results of all antenatal and postnatal investigations were entered in a spreadsheet for analysis. The Chi square test (or Fisher exact test when sample size was small) was used to compare proportions. The incidence rate (with 95% confidence intervals) of urinary tract anomalies in foetuses with hydronephrosis at different pregnancy stages was calculated, as well as the incidence rate ratio (with 95% confidence intervals) of urinary tract anomalies for third trimester dilatation compared with the 20-week scan. A Chi square test for linear trend was calculated to compare the proportion of anomalies diagnosed when hydronephrosis was diagnosed at 20, 28 weeks and in the third trimester. All statistical tests were performed with the package Stata 8 (Stata Corp, Texas, USA) and significance was defined by a two-tailed p value <0.05.

The study has been approved by our institutional ethics committee which has waived the requirement for informed consent as it was a retrospective notes review. The study has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

Results

A total of 4922 routine 20-week anomaly ultrasound scans were carried out (Table 1). Hydronephrosis was diagnosed in 97 foetuses (2%), of which 81.4% were males. Most were bilateral (73.2%) and less than 10 mm (90.7%). Ten women defaulted from follow up and in the 87 pregnancies who had a repeat scan at 28 weeks, hydronephrosis persisted in 44 foetuses (group A): 68.2% were males, most dilatations were bilateral (68.2%) and less than 10 mm (68.2%). As per the guidelines, only those 44 with persistent hydronephrosis at 28 weeks underwent postnatal imaging studies. One infant had a bilateral VUR (2 grade IV refluxing units), another had a unilateral pelvi-ureteric junction obstruction (PUJO), none had MCDK and 12 had idiopathic dilatation (19 renal units). The incidence rate of anomalies with hydronephrosis at 20, 28 weeks and in the third trimester are shown in Table 2. Surgery was required in only 1 infant with unilateral PUJO. All other affected children were managed conservatively with prophylactic antibiotic therapy as described earlier. No infant in this group developed UTI.

In the third trimester, hydronephrosis was diagnosed incidentally in 12 pregnancies (group B), of which 8 (two-thirds) had a normal 20-week scan previously and 4 (one third) had not been scanned earlier in view of late pregnancy booking. Most were males (66.7%); the dilatation was unilateral in 58.3% of cases and was less than 15 mm in the majority. The median gestational age at diagnosis was 32 weeks (range 29 to 36 weeks). All 12 foetuses underwent postnatal imaging studies: 2 had VUR (3 refluxing units: 1 grade II and 2 grade III reflux), one had MCDK (1 renal unit), another infant had PUV with absent right kidney and 5 had idiopathic dilatation (7 renal units). Surgery was required in only 1 infant with PUV and all other affected children were managed conservatively with prophylactic antibiotic therapy. No infant in this group developed UTI.

From all 56 infants (44 hydronephrotic at 20 weeks and 12 in the trimester) who underwent postnatal imaging, 41 had persistent hydronephrosis (table 2). The comparison between group A and B of the urinary tract anomalies diagnosed by imaging studies after birth and stratified by the antenatal APPD size is shown in table 2, including those requiring surgical treatment.

The prevalence rate of anomalies with hydronephrosis at 20, 28 weeks and in the third trimester are compared in Table 3. Pelvic dilatation size > 10mm (p=0.02), VUR (p=0.03) and idiopathic dilatation (p=0.02) were significantly more prevalent at the 3rd trimester scan. Of the 8 infants who had an earlier normal scan at 20 weeks, 2 had VUR (3 refluxing units: 1 grade II and 2 grade III reflux), one had a MCDK, another had PUV with absent right kidney, and 3 had idiopathic dilatation (4 renal units). In this subgroup, the incidence rate of VUR was therefore 25%, PUJO 0%, MCDK 8.3% and 41.7% had idiopathic dilatation. Surgery was required in only 1 infant with PUV. All other affected children were managed conservatively. The only child with parenchymal defect and the only infant with PUV were diagnosed by a scan after 28 weeks.

The relative risk of having VUR was 16.6 times higher (95% confidence intervals 0.80- 953.9) for dilatation diagnosed in the third trimester (risk of 16.7) compared to the baseline 20-week scan (risk defined as1) and this difference was significant (p=0.04) as shown in table 3.

Table 1. Comparison of 20-week, 3rd trimester scan and postnatal findings- Number (%)

	Group A		*Group B*	*p**	**Postnatal**
Timing of ultrasound	***20 weeks***	***28 weeks***	***3rd trimester***		
Subjects scanned	4922	87	NA	NA	56
Foetuses with hydronephrosis	97	44	12	NA	41
Bilateral	71 (73.2)	30 (68.2)	5 (41.7)	0.1	19 (46.3)
Unilateral	26 (26.8)	14 (31.8)	7 (58.3)		22 (53.7)
Dilatation size (mm)					
<10	88 (90.7)	30 (68.2)	5 (41.7)	0.02	30 (73.2)
≥10 to <15	9 (9.3)	14 (31.8)	5 (41.7)		7 (17.1)
≥15 to >20	0	0	0		2 (4.9)
≥20	0	0	2 (16.7)		2 (4.9)
Sex **Males**	79 (81.4)	30 (68.2)	8 (66.7)	1.0	32 (78)
Females	15 (15.5)	14 (31.8)	4 (33.3)		9 (22)
VUR **Infants**	1(1)	1 (2.3)	2 (16.7)	0.03	3 (7.3)
Renal units	2 (1)	2 (2.3)	3 (12.5)	0.01	5 (6.1)
Refluxing units [grade]	2 [IV]	2 [IV]	1 [II], 2 [III]		1 [II], 2 [III], 2 [IV]
MCDK	0	0	1 (8.3)	0.1	1 (2.4)
PUV	0	0	1 (8.3)	0.1	1 (2.4)
PUJO	1 (1)	1 (2.3)	0	0.8	1 (2.4)
Idiopathic dilatation ***Infants***	12 (12.4)	12 (27.3)	5 (41.7)	0.02	17 (41.5)
Renal units	19 (19.6)	19 (21.6)	7 (29.2)	0.01	26 (31.7)

NA: not applicable, VUR: vesico-ureteric reflux, MCDK: multicystic dysplastic kidney, PUV: posterior urethral valve, PUJO: pelvi-ureteric junction obstruction. *: Chi square test (Fisher exact test if n<5)

Table 2. Urinary tract anomalies (number of renal units) diagnosed after birth and stratified by antenatal APPD size (group A/group B)

APPD	*VUR*	*MCDK*	*PUJO*	*PUV*
<5mm	0/0	0/1	0/0	0/0
≥5 and <10 mm	2/2	0/0	0/0	0/1
≥10 and <15 mm	0/0	0/0	1/0	0/0
≥15 mm	0/1	0/0	0/0	0/0
Total	**2/3**	**0/1**	**1*/0**	**0/1***

APPD: antero-posterior pelvic diameter, VUR: vesico-ureteric reflux, MCDK: multicystic dysplastic kidney, PUJO: pelvi-ureteric junction obstruction, PUV= posterior urethral valve. **Required surgical treatment.*

Table 3. Risk (%) of urinary tract anomalies (95% confidence intervals) diagnosed following hydronephrosis at different pregnancy stages.

SCAN TIMING	*VUR*	PUJO	MCDK	IDIOPATHIC DILATATION
20 weeks	1.0 (0.05-6.4)	1.0 (0.05-6.4)	0	12.4 (6.5-20.6)
28 weeks	2.3 (0.06-12.0)	2.3 (0.06-12.0)	0	27.3 (14.9-42.8)
3rd trimester	16.7 (2.10-48.4)	0	8.3 (0.2-38.5)	41.7 (15.2-72.3)

VUR: vesico-ureteric reflux, PUJO: pelvi-ureteric junction obstruction, MCDK: multicystic dysplastic kidney

However severe reflux was more commonly diagnosed on early scan: one child with bilateral grade IV reflux was diagnosed at the 20-week scan and 2 infants with less severe VUR (grade II and III reflux) were diagnosed in the third trimester. The relative risk for VUR showed a significant increasing linear trend (p=0.01) when hydronephrosis was diagnosed at 20, 28 weeks and in the third trimester (table 3). There was no correlation between antenatal pelvic size and the prevalence of urinary tract anomalies (p>0.05). Idiopathic dilatation consisted of 41.7% of cases with dilatation in the third trimester and only 27.3% when hydronephrosis was discovered at 20 weeks. The risk of idiopathic dilatation was 3.4 times higher (95% confidence intervals 0.90- 10.3) for dilatation diagnosed in the third trimester compared to the 20-week scan, this difference was significant (p=0.05). The relative risk for idiopathic dilatation showed a significant increasing linear trend (p=0.003) when hydronephrosis was diagnosed at 20, 28 weeks and in the third trimester (Table 3).

Discussion

Routine 20-week anomaly scan is recommended in all pregnancies [1]. Most discovered antenatal hydronephrosis are transient and approximately 75% resolve spontaneously during pregnancy or after birth [3-7]. Little is known about hydronephrosis discovered late in pregnancy [14]. Our data show that urinary tract anomalies were more readily diagnosed by antenatal hydronephrosis discovered after 28 weeks than in the recommended 20-week prenatal ultrasound scan. This observation is also supported by the significant increase in the trend in the relative risk of urinary tract anomalies between hydronephrosis at 20 weeks and more advanced stages of pregnancy. The incidence of VUR in infants with persisting postnatal hydronephrosis was 7.3%, lower than in other reports [15, 16]. This could be explained by the fact that, unlike other studies, we did not perform cystography in the absence of postnatal dilatation, and may have therefore missed few infants with reflux. Another possibility is that, with the exclusion of foetuses with multiple congenital anomalies from the analysis, VUR was under-reported as it is likely that such abnormal foetuses may have a higher incidence of hydronephrosis and VUR [17]. Although in this study more cases of VUR were diagnosed on third trimester scan, those were of a less severe grade (II and III). It is reassuring that up to 75% of mild and 37% of severe VUR have been shown to resolve spontaneously by the age of four years [18].

The proportion of male foetuses with hydronephrosis was higher at 20 weeks but progressively declined at 28 weeks and in the third trimester. The reason for this is not clear. Although it may be a non-significant finding related to the small sample size, we could not compare with other studies as none have previously looked at the association between gender and antenatal hydronephrosis. The incidental diagnosis in the third trimester of PUV and unilateral renal agenesis in an infant with a prior normal 20-week antenatal scan could be attributed to a missed diagnosis. However this is unlikely as all scans were performed by qualified and experienced sonographers who, in fact, diagnosed more hydronephrosis at 20 weeks (1.97% of pregnancies) than in other reports (0.6%) [4, 12]. It is also possible that, in that same infant, the foetal bladder was not properly visualised or was of normal size at 20 weeks in view of the physiological limited foetal urine production which normally increases after 33 weeks of gestation [19]. The absent kidney in the third trimester could be related to the presence of dysplastic kidney tissue, still visible by ultrasound at 20 weeks, with subsequent involution during pregnancy when subsequent scans cannot visualise it anymore [20] .

Hydronephrosis may be diagnosed later in pregnancy or even post-natally in infants with prior normal antenatal scans [12, 21]. A study reported that scanning after 28 weeks of gestation in 313 pregnancies found 55 foetuses with renal anomalies, with a prevalence of VUR of 3.6 per 1000, much less than in our study, while obstruction was diagnosed in 6 per 1000 [22]. As many hydronephrosis seen in early pregnancy are transient, it is conceivable that dilatation seen in late pregnancy are likely to be more permanent and therefore more significantly associated with urinary tract anomalies. Increased urine output in third trimester may highlight dilated tracts that were not visible earlier when urine output was low, as it is known that foetal urine production doubles between 32 and 39 weeks compared to a modest increase of 15-25% in renal size [19]. This may explain that less than 10% of renal anomalies are detected before 17 weeks of gestation, while up to 91% are detected by 33 weeks [23].

The strengths of the project include the fact it was an unselected cohort study, the scanning was performed by a small group of qualified sonographers, comprehensive ultrasonographic and paediatric management protocols and guidelines have been implemented, ensuring a coherent plan for follow up and investigations. Several audits of the service have shown that the incidence of antenatal hydronephrosis has been relatively stable over the past few years in our institution. This seems to be largely explained by the fact that all antenatal scanning were being performed exclusively by a small group of qualified and accredited sonographers who followed a comprehensive ultrasonographic protocol, resulting in an increased sensitivity and accuracy of the scanning.

The study, however, also had weaknesses. One of the limitations is the small overall number of infants with uropathies, as found also in many other studies.[12,13,21] A larger sample size of foetuses

with hydronephrosis would have allowed a more precise estimate of the prevalence of uropathies with narrower confidence intervals. Another weakness is the fact that foetuses whose dilatation resolved at 28 weeks gestation and those with a normal postnatal ultrasound did not undergo postnatal uroradiological imaging, potentially resulting in some urinary tract anomalies being missed. In addition, the denominator for all incidental third trimester scans was not available because many were not performed by the trained antenatal sonographers and therefore were not recorded in their log book unless specifically referred to them when antenatal hydronephrosis was suspected. Furthermore, not all pregnancies which underwent a 20-week scan were scanned again in the third trimester. For both these reasons, the calculation the sensitivity, specificity, positive and negative predictive values of 20-week scan and third trimester scan was not possible. The confidence intervals for the relative risk of anomalies and for the rate ratio of anomalies were large because of the small sample size. Studies with much larger sample size are needed to have enough power to detect a statistically significant difference. Furthermore, the exclusion of multiple congenital anomalies may have biased the results as it is likely that such abnormal foetuses (some with hydronephrosis) would be diagnosed at 20 weeks and therefore less likely to be diagnosed later in pregnancy [17]. It is also conceivable that not all urinary tract anomalies were antenatally diagnosed by ultrasound, regardless of the stage of pregnancy, leading therefore to an underestimation of the prevalence of renal anomalies.

Although the scan at 20-weeks of gestation may be the best opportunity to diagnose aneuploidy and other anomalies, our data suggest that this timing may not be the best to detect urinary tract abnormalities as it misses significant urinary tract anomalies which can be diagnosed on a third trimester scan. However, in view of the small sample size in our study, larger studies, multicentre or through a national registry for antenatal hydronephrosis, are needed. Should they validate our results, a review of the appropriateness of the timing of the anomaly scan at 20 weeks of pregnancy would then be indicated. In the meantime, we can only recommend that during any opportunistic scan in the third trimester of pregnancy, even with a prior normal 20-week scan, hydronephrosis should always be looked for, as its presence at that stage is more likely to be associated with urinary tract anomalies.

In summary, renal tract anomalies are better predicted by foetal hydronephrosis detected in the third trimester than the recommended routine 20-week anomaly scan which may be falsely reassuring. These findings emphasize the need to always look for renal dilatation during incidental antenatal scans in the third trimester, even if prior scans were normal.

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