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EVALUATION OF FETAL AND NEONATAL ULTRASOUND OF KIDNEY, URETER AND BLADDER FOR THE RISK OF VESICOURETERAL REFLUX AT A TERTIARY CARE HOSPITAL OF NORTH INDIA

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ABSTRACT

PURPOSE: To analyze the relationship between foetal and postnatal anteroposterior diameter of renal pelvis dilatation (RPD) and the presence of vesicoureteral reflux.

METHODS: The study was a prospective observational study conducted in the Department of Paediatrics of associated hospital of Government Medical College, Srinagar, Jammu and Kashmir. Patients included were all the pregnant ladies whose fetal USG shows the presence of antero-posterior diameter (APD) of renal pelvis >4mm in second trimester or >7mm in third trimester.Only patients in whom abnormalities persisted as moderate unilateral hydronephrosis, bilateral mild hydronephrosis, having lower ureteral dilatation on USG scan or UTI during neonatal period had Voiding Cystourethrography (VCUG) at 6 weeks of life to rule out vesicoureteral reflux (VUR).

RESULT: Out of 119 patients, 98 patients were available for further analysis who had fulfilled the inclusion and exclusion criteria's. Antenatal Hydronephrosis(ANH) was detected more often in males (80.61%)than in females (19.39%). More than two-thirds of patients had mild ANH, & more than two-thirds had unilateral ANH. The first postnatal ultrasound scan showed normalization of the RPD in 58 patients (59.18%) and persistence in 40 patients (40.82%). Patients having mild bilateral hydronephrosis and all those with moderate and severe dilatation of RPDs were put on antibiotic prophylaxis after first post-natal scan. In spite of prophylactic antibiotic therapy the proportion of UTI among moderate & severe cases of PNH was significantly higher than those of mild cases & cases with no PNH. 88.78% patients showed normalization of the RPD at 6 months ultrasound scan while rest had mild to severe dilatation of the RPD. 21 patients (65.6%) were found to have VUR on VCUG out of 32, with 4 of them having bilateral VUR. **CONCLUSION:** It is very important to identify patients who require emergent postnatal evaluation before discharge, as these patients are at higher risk for poor outcomes.

KEYWORDS : Fetal, Neonatal, Antenatal Hydronephrosis, Vesicoureteral Reflux

INTRODUCTION:

Congenital abnormalities of the kidneys and urinary tract (CAKUT) are the most common abnormalities detected during routine prenatal fetal ultrasound [1]. CAKUT make up one of the largest groups of congenital anomalies amenable to neonatal care representing 0.2-2 % of all new-borns [2]. It has been observed, that antenatal hydronephrosis (ANH) accounts for 50% of the anomalies detected by prenatal ultrasound (US), and the estimated prevalence of ANH is around 2.5-5% during the second trimester [3,4]. Although the presence of a renal pelvic dilation (RPD) is often a physiological state, nevertheless it has been associated with congenital urinary tract anomalies requiring intervention in 4.1-15.4% [5,6]. The rates of vesicoureteric reflux (VUR) and urinary tract infections (UTI) are several-fold higher among the ANH patients [7]. The antenatal ultrasound screening is most commonly performed at 18-20 weeks of gestation. This is the time when the renal architecture becomes visibly distinct. Normally the renal pelvis and calyces are not seen, if seen then it indicates hydronephrosis. The sonologist should be vigilant in the antenatal period to differentiate a dilated collecting system from the hypoechoic sonolucent pyramids which may mimic hydronephrosis. Once the diagnosis of a dilated collecting system is made, it should be objectively described using one of the various classification systems. The majority of authors use ether the Antero posterior diameter (APD) system or the Society of Fetal Urology (SFU) classification. In the early 80's a threshold value of 10 mm of pelvicalyceal system indicated the need for further investigations during the postnatal period. This was further substantiated by the work of Corteville et al, while a number of other studies have noted persistent postnatal uropathy when the APD measures > 6 mm at <20 weeks (wk), >8mm at 20-30 weeks and> 10 mm at >30 weeks of gestation [8,9]. Recently cut off of 6 mm at 20 wk and 10 mm at 30 wk have been suggested for pyelectasis and an APD cut off of 10 mm at 20 wk and 12 mm at 30 wk for hydronephrosis [10].

Vesicoureteral reflux (VUR) is the upward flow of urine out of the bladder and into the ureters often to calyces during voiding. It is thought to be caused by the developmental anomaly at the ureterovesical junction in which ureteral orifice may be lateralized or too large or the submucosal ureter is too short or deficient in the longitudinal muscle fibres. Immaturity of the ureterovesical junction may contribute to some extent. Patients with VUR can present in the neonatal period with antenatally detected hydronephrosis [11]. A common cause of antenatal hydronephrosis, VUR is found in up to 38% of infants, even in the setting of a normal postnatal ultrasound [4]. The severity of reflux is classified as mild(Grades I and II)moderate(Grade III),severe(Grades IV and V).

Vesicoureteral reflux (VUR) is risk factor for recurrent UTIs and pyelonephritis which can cause renal parenchymal scarring resulting in hypertension and /or renal insufficiency [12]. Although spontaneous resolution of VUR occurs in 78-90% of grade I-III VUR, but grade IV and V-VUR usually require surgical intervention and at times can resolve of its own [13]. It is important to distinguish infants with transient hydronephrosis and minimum need for invasive investigations from those

suffering from significant illness that require long-term follow up or surgery. For the related reasons studies have focused on RPD and VUR, while lesser number of studies were conducted specifically focused on the relation between the degree of the APD and the risk of VUR. In this prospective study, we analysed the US relationship between the antenatal and postnatal kidney, ureter and bladder and association of VUR in this regard.

Purpose:

This study was conducted to analyze the relationship between foetal and postnatal anteroposterior diameter of renal pelvis dilatation (RPD) and the presence of vesicoureteral reflux.

METHODS

The study was a prospective observational study conducted at Postgraduate Department of Paediatrics G. B. Pant Hospital and LD Hospitals, associated hospitals of Government Medical College, Srinagar, Jammu and Kashmir over a period of one year with effect from December 2019 to November 2020.
Inclusion criteria: All pregnant ladies whose fetal USG shows the presence of antero-posterior diameter (APD) of renal pelvis >4mm in second trimester or >7mm in third trimester(Table 1).

Exclusion criteria: Patients with non-urological congenital anomalies, duplex system, renal cysts, chromosomal anomalies, missing antenatal data or incomplete follow-up will be excluded.

Table 1: Degree of Antenatal Hydronephrosis(ANH) according to Renal Pelvis Anterior-posterior Diameter (APD) Adjusted for Gestational Age:

Degree of ANH	APD at 2nd trimester	APD at 3rd trimester
Mild	4-7mm	7-9mm
Moderate	7-10mm	9-15mm
Severe	>10mm	>15mm

All newly born patients whose fetal USG would be suggestive of hydronephrosis had undergone successive USG scans of urinary tract on 7th, 30th, 45th day of life.

The infants was categorized according to the APD as follows:

1. Normal (0–4 mm),
2. Mild(5–9 mm),
3. Moderate (10–15 mm) and
4. Severe (>15 mm).

Only patients in whom abnormalities persisted as moderate unilateral hydronephrosis, bilateral mild hydronephrosis, having lower ureteral dilatation on USG scan or UTI during neonatal period had Voiding Cystourethrography (VCUG) at 6 weeks of life.

Criteria for an abnormal postnatal ultrasound was ;

- Pelvic diameter ≥4 mm
- Calyceal or Ureteraldilatation (ureteral diameter >2 mm),
- Pelvic or Ureteralwall thickening,
- Absence of the corticomedullary differentiation and
- Signs of renal dysplasia (small kidney, thinned or hyperechogenic cortex and cortical cysts)

Vesicoureteral reflux (VUR) was graded according to the International Reflux Study Committee classification. Because of the benign evolution of grade I and II VUR, VUR was classified into two groups: mild-moderate (I–II) and severe (III–V). Patients with bilateral VUR or bilateral dilatation were categorized into the higher grade of VUR or dilatation and were put on antibiotic prophylaxis using amoxicillin (10 mg/kg/day), from birth and were put on trimethoprim (2mg/kg/day) at 3 months. The antibiotic prophylaxis was discontinued in patients without VUR on VCUG and in those with RPD <10 mm. Those who have two consecutive ultrasound scans normal and in children without VUR based on the results of the VCUG were taken as normal and their follow up was stopped at 45 days. The children with persistence of a dilatation were followed with repeated ultrasounds at 3 and 6 months after birth. The clinical course at 6 months was analysed and recorded for all children either by means of the clinical follow-up or a phone questionnaire for patients whose follow-up was stopped at 1 month. The postnatal ultrasound examinations will be performed by senior radiologist using Seimens Acuson X-300, USA, Model-KT-LM-200 HDPE.

Statistical Methods

The data was entered into Microsoft Excel 2010 and analyzed using statistical package for social sciences (SPSS Ver. 23). Categorical variables were described as frequency and percentage. Chi-square was used to see the association between two categorical variables. Whenever chi-square was not feasible Fischer exact test was used in its place. Bar charts and Pie charts were used to describe the data in a presentable form. A p value of 0.05 was considered to be statistically significant.

RESULTS:

A total of 61587 patients had attended the out patients department of LD and GB Pant Hospital during the study period. Out of which, 10800 underwent ultrasound scanning for fetal wellbeing. 432 patients had fetal anomalies including 119 having antenatal hydronephrosis and 313 having other fetal anomalies. Out of 119 patients, 21 were excluded from the study , 16 because of loss of follow up and 6 refused to undergo VCUG and only 98 patients were available for further analysis who had fulfilled the inclusion and exclusion criteria's. Antenatal Hydronephrosis was detected more often in males (80.61%)than in females (19.39%) (fig.1).

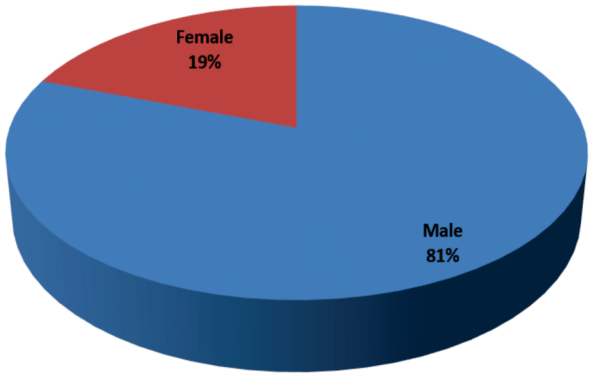

Fig 1. Pie chart depicting gender distribution.

More than two-thirds of patients had mild ANH, & more than two-thirds had unilateral ANH. 10 % of ANH cases detected at 2nd trimester had normalized at 3rd trimester. The first postnatal ultrasound scan showed normalization of the RPD in 58 patients (59.18%) and persistence in 40 patients (40.82%). Patients having mild bilateral hydronephrosis and all those with moderate and severe dilatation of RPDs were put on antibiotic prophylaxis after first post-natal scan. 2nd postnatal ultrasound showed normalization of RPD in 67 patients and persistence in 31 patients. In spite of prophylactic antibiotic therapy, the proportion of UTI among moderate & severe cases of PNH was significantly higher than those of mild cases & cases with no PNH. Thus more the severity of PNH at 7th day more the chances of UTI. A total of 75(76.53%) patients resolved, while 23(23.47%) patients showed persistence of the RPD at 45th day of life (3rd postnatal ultrasound scan). 32 patients underwent VCUG out of which 21 had VUR. About

19% of VUR were bilateral in nature. There was a significant correlation between the degree of ANH and Postnatal VUR as p value is <0.001 using Fisher's Exact method**(Table 2).**

Table 2.Relationship between degree of ANH and Postnatal VUR

Degree of ANHat 2nd Trimester	Post-natal VUR on VCUG		Total	Percentage of VUR (%)
	Present	Absent		
Mild (4-7mm)	1	65	66	1.51
Moderate (7-10mm)	10	9	19	52.63
Severe (>10mm)	10	3	13	76.92
Total	21	77	98	21.43

At 3 months of life, the resolution of RPD was 81.63% . 88.78% patients showed normalization of the RPD at 6 months ultrasound scan while rest had mild to severe dilatation of the RPD. Bar chart showing comparative USG diagnosis of Hydronephrosis at different stages of study(Fig.2)

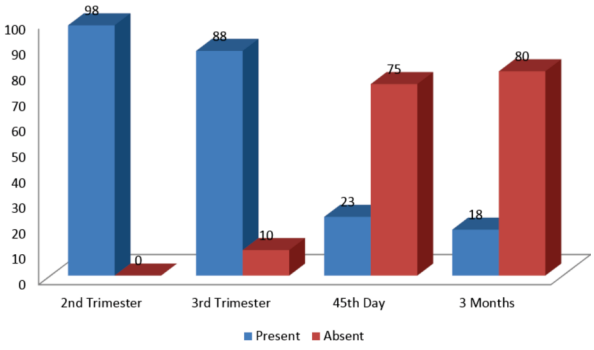

Fig.2: Bar Chart depicting comparative USG diagnosis of Hydronephrosis at different stages of study

21 patients (65.6%) were found to have VUR on VCUG out of 32, with 4 of them having bilateral VUR(Table 3).

Table 3:Distribution of vesicoureteral reflux according to antenatal and postnatal Renal pelvic dilatation in patients undergoing voiding cystourethrography (VCUG)

Renal Pelvic Dilatation	Low grade VUR(I-II)		Severe grade VUR(>II)		No VUR	Total
	Unilateral	Bilateral	Unilateral	Bilateral		
Mild (5-9 mm)	1	-	-	-	3	4
Moderate (10-15 mm)	6	-	2	2	7	17
Severe (>15 mm)	1	-	7	2	1	11
Total	8	0	9	4	11	32

DISCUSSION:

Antenatal hydronephrosis (AHN) has become one of the most commonly detected ultrasound (US) findings, during the second or third trimester of pregnancies. Isolated renal pelvic dilatation can be an early sonographic sign of fetal hydronephrosis or a marker of other abnormalities, such as renal duplication or VUR, which cannot be identified easily by ultrasonography during pregnancy [14]. In such situations the patient is being examined by the pediatric nephrologist/urologist before the birth of the baby with a predetermined plan. Antenatal hydronephrosis (ANH) is the most common abnormality detected prenatally found in 1% to 5% of all foetuses [15,16]. The rate of detection of ANH has increased significantly due to increased use of prenatal ultrasound [17]. Our study revealed males predominance 79(80.6%), as compared to females 19(19.3%), with a male female ratio of 4.1:1. This male preponderance is similar to the study conducted by Ismaili K et al, who studied a total of 16,929 antenatal ultrasound scans between October 1998 and October 2000 in an unselected population of pregnant women. The prenatal diagnosis of renal pelvis dilatation without concomitant anomaly was made in 4.5% of 5643 fetuses. The male/female ratio was 2:1 (85 female infants) among the 258 fetuses.

By taking the anteroposterior pelvis diameter of ≥4 mm in second trimester and ≥7mm in third trimester of pregnancy, we found the incidence of AHN was 1.01%, among all OPD and IPD patients. This is in accordance with the study by Langer B et al; where mean renal pelvis dimension >5 or 10 mm before or after 28 weeks of gestation, respectively was taken as pyelectasis, and an estimated incidence 0.60% of urinary tract malformations was observed [18]. A similar result was obtained by Odibo AO et al, who in their observation found during the during the 3-year study period, that out of 7416 women, 150 cases had pyelectasis on prenatal US, giving a prevalence of 2% [19].

However, our incidence of ANH was quite lower than the findings of Ismaili K et al, who found that 4.5%, study population on US scans show renal pelvis dilatation without concomitant genitourinary anomaly. The difference could be because of the their large sample size, spanning over a study period of a 24-month period, during which there were 5643 births.

In a cohort of 144 infants with mild hydronephrosis on first post-natal ultrasound, Barbosa et al, reported resolution of mild hydronephrosis in 46.5% of children and stability in 47.2% and progression to surgical intervention in 6.3%. [20].

Tombesi et al, who in their study detected mild isolated antenatal hydronephrosis in 193 newborns (109 unilateral, 84 bilateral; 23 (12%) had UTI and 2 of them showed low-grade reflux. After a mean follow-up of 15 months, 91 renal units showed intrauterine resolution (33%), 111 (40%) total resolution, 20 (7%) partial resolution, 52 (19%) stability and 3 (1%) progression. They concluded resolution rate of 73% and progression of 1% in a their study cohort [21].

The intervals of repeat US scanning among our patients was 2 months after the first prenatal scan, followed by postnatal scans at day 7, 30, 45, 90, and at completion of 6 months. The rate of resolution was quite comparable to the earlier studies. Alconcher et al reported that 80% of units resolved within the first 12 months of life. Others have reported intervals to resolution of 13.4 months–17 months [22].

Among the 98 children, 40 underwent VCUG, among whom VUR was identified in 21 (21.40%) patients. Our results are comparable with the study conducted by Brogen and Cheyinde (20.68%) [23], but much higher than the studies conducted by Gunn et al 64(3.22%) [24], and Afroz R et al 72 (2.70%) [25](Table 4).

Table 4: Comparison with the past studies regarding the occurrence of VUR among ANH patients

S. no.	Studies	Antenatal hydronephrosis cases	Vesicoureteral reflux(n)	Percentage (%)
1.	Brogen and Chiyande ,2000 23]	29	6	20.68
2.	Gunn et al ,1988 [24]	62	2	3.22
3.	Afroz R et al, 2016 [25]	111	3	2.70
4.	**Present study**	**98**	**21**	**21.4**

VUR was observed in 1(25%) mild PNH patient, 10 (58.8%) moderate PNH patients, and 10 (90.9%) of severe PNH

patients, a statistically significant observation (p-value<0.05). This is in conformity with the observations made by the Grazioli S et al. where in they found the proportion of children with VUR increased with increasing postnatal RPD. The odds ratios were 5.0 (95% CI 0.5–51.2) for children with a postnatal RPD 7–9 mm compared to the children with a postnatal RPD 0–6 mm, and 9.1 (95% CI 1.0–80.9) for children with a postnatal RPD ≥ 10 mm. However these findings are in contradiction with the series of Phan et al. [26] in which the postnatal ultrasound was unable to predict the presence of VUR. This difference can possibly be explained by the fact that in the study of Phan et al., the comparison was based on a single ultrasound. Our results show that the application of a protocol which includes a selection of children for VCUG on the basis of the results of postnatal ultrasounds represents a safe strategy for children with ANH and avoids unnecessary invasive and irradiating examinations.

Sub-analysis of our results showed that VUR grade I-II was found in 8(32%), Grade III in 09 (36%), Grade IV in 07(28%), and Grade V in 1 (4%) .From these observations, an increase in RPD the chances of rate of occurrence and grade of VUR progressively increases. These findings are similar to the observations made by Aboutaleb H et al observed that among 308 patients categorized as mild (grade 1 to 2) or moderate/severe (grade 3 to 4). VUR was grade I in 44 cases, II in 145, III in 203 and IV to V in 84 . Preoperative HN existed in 123 refluxing units, and was mild in 4 (9%), 11 (7.5%), 39 (19%) and 28 (33%), and moderate/severe in 0, 2 (1.4%), 14 (7%) and 25 (30%) of grade I, II, III and IV to V VUR cases, respectively. The degree of preoperative HN correlated with VUR grade (p <0.0001). At 15 months postoperatively HN resolved in 80 units (65%) and persisted in 43 (35%) [27].

CONCLUSION

ANH is a common condition with variable clinical outcomes. The most common type of ANH is transient mild dilation that requires routine outpatient ultrasound evaluation. However, it is very important to identify patients who require emergent postnatal evaluation before discharge, as these patients are at higher risk for poor outcomes. Postnatal renal ultrasound, use of narrow spectrum antibiotic prophylaxis and VCUG are being used more selectively to avoid misuse and overuse in these. The effectiveness of prophylactic antibiotics in preventing UTIs remains unproven, and routine use is recommended only in patients at increased risk for UTI. Our data support the use of immediate antibiotic prophylaxis while awaiting initial postnatal US and favours VCUG procedure in infants with a history of PNH and postnatally persistent bilateral mild hydronephrosis, moderate and severe forms of hydronephrosis.

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