

## Fetal Hydronephrosis in the Second and Third Trimester of Pregnancy and Six Months Follow-up after Birth

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### ABSTRACT

**Background:** Prenatal hydronephrosis (PNH) may be associated with congenital abnormalities in the urinary tract. This study aimed to determine and follow up on the fetus diagnosed with PNH until the first six months after birth.

**Methods:** This prospective longitudinal study was conducted from May 2021 to July 2022 in fetuses who were diagnosed with PNH based on the size of the anterior-posterior diameter of the renal pelvis (APRPD) by a perinatologist with an S W 80 ultrasound machine. If it is  $\geq 4$  mm in the 2nd and  $\geq 7$  mm in the 3rd trimesters, it is considered PNH. These infants were followed up until the first six months after birth. Data analysis was performed using SPSS 20, Chi-square, Fisher's exact, and T-tests.

**Results:** Of the 56 eligible fetuses, 50 fetuses were followed up. The mean gestational age at the time of diagnosis of PNH was  $20.48 \pm 5.37$  weeks. Twenty cases of PNH (45.45%) spontaneously improved until birth. Thirty cases had hydronephrosis in the first week after birth, 16 of which (53.33%) were bilateral. The cause of PNH in 90% is idiopathic. Other causes include polycystic kidney, vesicoureteral reflux, and posterior urethral valve. One case died in the first week after birth. Forty-three cases had spontaneous recovery of PNH by six months, and 6 cases (12%) had adverse outcomes. The severity of PNH in the 3rd trimester had a significant relationship with adverse outcomes ( $P=0.001$ ). The APRPD in the 3rd trimester has more sensitivity and specificity than in the 2nd trimester for predicting adverse outcomes after birth.

**Conclusion:** In most cases, the cause of PNH is idiopathic, and the resolution of PNH occurs up to 6 months after birth. Moderate and severe PNH was associated with a poorer outcome and requires more follow-up and intervention.

**Keywords:** Complication, Fetal hydronephrosis, Fetal pyelectasis, Perinatal outcome

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## Introduction

Prenatal hydronephrosis (PNH) is the abnormal expansion of the pyelocalyxal system in the fetus, the most common abnormal finding in prenatal ultrasounds (1, 2). Although sometimes it is a normal variant in mild cases (3). PNH is diagnosed in 1-2% of all pregnancies (4). In some studies, it has been reported up to 5% (5). The diagnosis of PNH is based on prenatal ultrasound, which has increased in recent years due to the advancement of ultrasound technology (6). PNH is diagnosed based on the size of the anterior-posterior diameter of the renal pelvis (APRPD) in a transverse view, the normal value of which depends on the gestational age of the fetus (1).

There are different opinions about the abnormal threshold of APRPD diameter; some researchers consider a diameter of more than 6 mm in late pregnancy to indicate PNH and recommend follow-up after birth (7). In a review study, the threshold values of APRPD for diagnosing PNH at a gestational age less than 28 weeks,  $\geq 4$  mm, and at a gestational age equal to or greater than 28 weeks,  $\geq 7$  mm have been mentioned (5). Another study suggested that these threshold values for gestational age are less than 30 weeks and  $\geq 30$  weeks, respectively (8).

In many cases, the cause of PNH cannot be determined before birth. The most common causes of PNH are ureteropelvic junction obstruction (UPJO), ureterovesical junction obstruction (UVJO), vesicoureteral reflux (VUR), and ureterocele and posterior urethral valve (PUV) (3). PNH can be unilateral or bilateral. The cause of unilateral PNH is commonly stenosis or obstruction of the connection between the ureter and the pelvis. Common causes of bilateral hydronephrosis in boys are mostly obstruction due to the posterior urethral valve, and in girls, obstruction caused by ureterocele (9).

After birth, the cause of PNH can be diagnosed with additional imaging, including voiding cystourethrography (VCUG) and a kidney scan. The prognosis of PNH depends on its cause (10). In some studies, PNH has been associated with obstetric complications such as oligohydramnios (1, 11). However, in another study, there was no significant relationship between PNH and oligohydramnios (12). For years, common congenital kidney diseases such as vesicoureteral reflux, ectopic kidney, and duplication were diagnosed when the patient had recurrent urinary tract infections only. Since urinary tract infection is the main and important cause of permanent kidney damage, it is expected that with recent

advances and prenatal diagnosis, these disorders can be diagnosed and treated before the patient experiences the first attack of urinary tract infection. It should be done correctly to prevent permanent and long-term kidney damage (2).

Considering the improvement of diagnostic equipment and cooperation between perinatologists and pediatricians and performing more ultrasounds of the fetus and early diagnosis of PNH in pregnancy, this study aims to determine and follow up the fetus with PNH in the second and third trimester of pregnancy until the first 6 months after births were performed in a tertiary referred and academic center of high-risk pregnancy.

## Methods

This prospective longitudinal study, which was approved by the Ethics Committee with the code (IR.MUBABOL.HRI.REC.1400.131), was conducted from May 2021 to July 2022 in Ayatollah Rouhani and Shafizadeh Children's Hospitals affiliated with the Babol University of Medical Science, Babol, Iran.

### Participants

This study was conducted on fetuses diagnosed with PNH during an ultrasound in the second or third trimester of pregnancy. If the parents provided written consent, they were included in the study, and the infants were followed up until the first six months after birth in terms of spontaneous recovery, supportive treatment, or the need for surgery.

### Sampling method

Sampling was done using a convenience sample and in the form of a census from when the proposal was approved until the number of samples was completed. The inclusion criteria included fetuses whose APRPD in the transverse view of the kidney in the second-trimester sonography was reported to be  $\geq 4$  mm and  $\geq 7$  mm in the third trimester (13). All pregnancy ultrasounds were measured by a perinatologist with a Samsung S W 80 ultrasound machine.

Exclusion criteria include parents' lack of consent for follow-up and treatment measures, the occurrence of intrauterine death (IUFD), and the presence of various other anomalies such as VACTERL syndrome, which is a combination of several anomalies: vertebral defects, anal atresia, cardiac defect, tracheoesophageal fistula, renal anomalies, and limb abnormalities. The minimum

sample size based on the prevalence of PNH in the study of Sairam et al., with a 15 % drop probability, has been calculated for 35 samples (14). However, 56 eligible samples were examined and followed up in this study.

In the present study, the valid standard of Society For Fetal Urology (SFU) was used for the diagnosis and severity of hydronephrosis in the second and third trimester of pregnancy and after birth, whose validity and reliability have been measured in previous studies (13).

Based on the Yalçınkaya et al. study, the severity of PNH was defined as mild, moderate, and severe grade (Table 1) (13).

**Table 1.** SFU classification system (13).

Classification of PHN	Second-trimester APRPD (mm)	Third- trimester APRPD (mm)
Mild	4-7	7-9
Moderate	7-10	9-15
Severe	>10	>15

SFU, Society of Fetal Urology; PHN, prenatal hydronephrosis; APRPD, anteroposterior renal pelvic diameter

### **Therapeutic and diagnostic procedures**

After coordinating with the midwife in the prenatal clinic of Ayatollah Rouhani Hospital, all fetuses diagnosed with PNH were introduced to the project manager and referred to the perinatology clinic. First, the research objectives were explained to the sample. To ensure the confidentiality of the information, eligible pregnant women were invited to participate in this study according to the inclusion and exclusion criteria. In the first visit, prenatal examinations like maternal weight and height measurements were performed after obtaining written consent. A midwife at the prenatal Clinic in Rouhani Hospital completed the socio-demographic and fertility factors checklist. In cases of bilateral hydronephrosis, in the presence of oligohydramnios, consultation with a perinatologist was done, and in the absence of oligohydramnios, ultrasound was performed every 2-6 weeks. In cases of bilateral PHN and oligohydramnios, a perinatologist was consulted; otherwise, ultrasounds were repeated every two to six weeks.

After birth, follow-up by ultrasound was done after the first week of life for mild PNH and the first 24 hours for moderate to severe PNH, or in cases where the neonate was a boy and had a distended bladder during the examination by a neonatal specialist. According to the ultrasound results, follow-up of the infants with kidney ultrasound and VCUG was done if needed. By taking the contact phone numbers of the parents, the researcher conducted follow-ups every four

weeks for six months after the baby's birth. It tried to answer all the mothers' or fathers' questions and concerns during the phone calls, and they were given sufficient explanations about the importance of monitoring the baby. The variables evaluated in this study include maternal age, maternal body mass index before pregnancy, fetal hydronephrosis diagnosed by size of the anterior-posterior diameter of the pelvis in the transverse view of the kidney, severity of fetal hydronephrosis, unilateral or bilateral fetal hydronephrosis, gestational age when fetal hydronephrosis was diagnosed, pregnancy complications in the current pregnancy such as premature delivery, stillbirth, prenatal mortality, preeclampsia, gestational diabetes, fetal growth restriction, gender of the infant, oligohydramnios, age at birth, birth weight, hospitalization of the infant in the NICU, need for resuscitation, respiratory distress syndrome and complications from neonate to the first six months after birth, including periodical ultrasound, the results of each period, supportive treatment, spontaneous recovery, and the need for surgery. The adverse outcomes after birth in this study included the lack of spontaneous recovery for up to six months, the need for surgery, the need for antibiotic prophylaxis, and death. A pediatric nephrologist first visited all infants with PNH, and to determine the cause of hydronephrosis in all cases after birth, renal ultrasound, VCUG, and renal scan were performed if needed.

### **Statistical Analysis**

Descriptive characteristics of patients with statistical indicators for quantitative variables with the default of normality using mean, standard deviation, minimum, maximum, 95% confidence interval, and nominal and rank qualitative variables were also presented with frequency and percentage. The Independent Samples T-test compares the equality of two means between qualitative variables with the assumption of the equality of variances. It checks the statistically significant relationship between qualitative variables from the Chi-square test, and Fisher's exact test was used in case of limitations in the expected frequency. To predict the adverse outcome after birth, the estimation of sensitivity, specificity, positive and negative predictive value, and accuracy were used. All analyses were done by SPSS software version 20, and the significance level ( $P < 0.05$ ) was considered.

### Ethical approval

In order to do ethical consideration, this study followed the guidelines set by the declaration of Helsinki and received ethical approval for the human subject by the Ethics Committee of Babol University of Medical Science approved the study. [Code of Ethics: IR.MUBABOL.HRI.REC.1400.131]. The pregnant women and partners provided written informed consent to participate in the study.

### Results

Of the 56 cases with PNH included, six cases were excluded due to non-cooperation, and finally, 50 cases were analyzed. Table 2 shows the demographic information of the patients.

Forty-four cases of PNH were diagnosed in the second trimester and six cases in the third trimester of pregnancy. The average gestational age at the time of diagnosis of PHN was  $20.48 \pm 5.37$ . Thirty-two of the 44 cases of PNH in the 2nd trimester showed bilateral PHN. Unilateral PHN was observed in 12 cases, with 6 cases on the right side and 6 cases on the left side.

Spontaneous resolution of PNH progressed to 20 fetuses in the 3rd trimester, and six new cases were diagnosed in the 3rd trimester. Of the 30 cases of PNH in the 3rd trimester, 16 fetuses had bilateral PNH, and 14 fetuses had unilateral PNH (8 cases on the right side and 6 cases on the left side).

The cause of PNH was idiopathic in most cases (90%). Other causes included polycystic kidney (n=2), ureterovesical junction obstruction (n=1), bladder-to-ureter reflux (n=1), and posterior urethral valve (n=1). Follow-up of all cases showed that spontaneous recovery of PNH occurred in 20 cases (40%) during the fetal period, 23 cases (46%) up to six months after birth, and 6 cases (12%) did not improve until the end of the study. Surgery was performed for one baby with a posterior urethral valve, and one baby

had premature delivery due to oligohydramnios and died after birth due to respiratory distress and pneumothorax in the first week of life.

The adverse outcome of PNH in this study was 14% (N=7), which included the lack of spontaneous recovery until six months after birth, the need for surgery, the need for prophylactic antibiotic treatment, and infant death.

According to this study's findings, unilateral or bilateral PNH in the second and third trimesters of pregnancy had no statistically significant relationship with the adverse outcome after birth. This study showed that the severity of PNH increased the probability of an adverse outcome. So, in the second trimester, moderate to severe PNH of 36.4% was associated with an unfavorable outcome ( $P=0.029$ ); however, in the third trimester, it increased to 58.3% ( $P=0.001$ ) (Table 3).

This study showed that if PNH is accompanied with and without oligohydramnios, the adverse outcome was 28.6% and 11.6%, respectively ( $P=0.25$ ). In terms of gender, in boys, the adverse outcome was almost twice as high as in girls (16.2% vs. 7.7%,  $p=0.660$ ), and also, in terms of the need for resuscitation, the group that needed resuscitation was almost four times more likely to have an adverse outcome than the other group. (40% versus 11.1%,  $P=0.138$ ). The group that needed to be hospitalized in the intensive care unit suffered adverse outcomes almost three times more than the other group (33.3% vs. 11.4%,  $P=0.192$ ). Also, infants who had at least one neonatal complication at birth had an adverse outcome almost two times more than others (25% vs. 11.9%,  $P=0.310$ ).

Regarding the association between adverse outcomes of PNH and maternal characteristics, the results indicated that in mothers with a body mass index above 25, the frequency of adverse outcomes was 16.7%. In contrast, in mothers with a body mass index below 25, it was 10%, but this

**Table 2.** Demographic and fertility characteristics of the researched samples in the study group (N=50)

Variable	Mean $\pm$ SD	95% confidence interval for the mean		Domain		
		Lower	Upper	Min	Max	
Age of mothers (years)	28.82 $\pm$ 5.04	27.39	30.25	17	42	
BMI of mothers (kg/m <sup>2</sup> )	25.58 $\pm$ 4.26	324.37	26.79	17.2	39.3	
Gestational age (at the time of PNH diagnosis)	20.48 $\pm$ 5.37	18.95	22.00	10	33	
Age of infants at birth (week)	838.04 $\pm$ 1.86	37.51	38.57	30	42	
Newborns Birth weight (grams)	3347 $\pm$ 604.77	3175.13	3518.13	1300	4700	
APRPD in the second trimester (mm)	Right	5.16 $\pm$ 1.82	4.64	5.67	2	10
	Left	5.12 $\pm$ 2.08	4.53	5.71	1	11
APRPD in the third trimester (mm)	Right	7.55 $\pm$ 2.81	6.75	7.91	3	16
	Left	7.15 $\pm$ 2.68	6.38	7.91	4	16

Abbreviations: BMI, Body mass index; APRPD, anterior-posterior diameter of the renal pelvis

**Table 3.** Comparison of unilateral and bilateral PNH and its severity with the outcome after birth (N=50)

Groups	Sub-groups	Outcomes		P value	
		Favorable N (%)	Un favorable N (%)		
PNH in the second trimester	Unilateral (6 cases on the right and 5 cases on the left)	11 (91.7)	1 (8.3)	0.664	
	Bilateral	27 (84.4)	5 (15.6)		
PNH in the third trimester	Unilateral (8 cases on the right and 5 cases on the left)	11 (78.6)	3 (21.4)	1.000	
	Bilateral	12 (75)	4 (25)		
Intensity of PNH	In the 2nd trimester	Mild	31 (93.9)	2 (6.1)	0.029
		Moderate to severe	7 (63.6)	4 (36.4)	
	In the 3rd trimester	Mild	18 (100)	0 (0)	
		Moderate to severe	5 (41.7)	7 (58.3)	

difference was not statistically significant ( $P=0.687$ ). Comparison between two groups of mothers with and without chronic medical disease showed that the frequency of adverse outcomes was 25% and 11.9%, respectively, but this difference was not statistically significant ( $P=0.310$ ).

In our study, the standard threshold of 4 mm APRPD in the second trimester and 7 mm in the third trimester to predict the adverse outcome, as well as the sensitivity and specificity along with the positive and negative predictive value and its accuracy in the samples were calculated (Table 4).

**Table 4.** Statistical indicators of pelvic diameter threshold for predicting adverse outcome after birth(N=50)

Variable			Sensitivity	Specificity	PPV	NPV	Accuracy
Threshold of APRPD as a predictor of adverse outcome	PNH in the second trimester (4 mm)	Right	57.14%	23.26%	10.81%	76.92%	28%
		Left	85.71%	25.58%	15.79%	91.67%	34%
	PNH in the third trimester (7mm)	Right	85.7%	53.48%	23.07%	95.83%	58%
		Left	100%	65.12%	31.82%	100%	70%

Abbreviations; APRPD, anteroposterior renal pelvic diameter, PPV, Positive predictive value; NPV, Negative predictive value

## Discussion

In this study, spontaneous recovery of PHN occurs in 40% of cases before birth, 46% of them recovered by six months of age, and only 14% of cases had adverse outcomes. In different studies, the rate of spontaneous recovery of PHN has been reported to be very different. Sen et al.'s study 53% (15), Shukla et al.'s study 54% (16), Loardi et al.'s study 36% (12), Elmaci et al.'s study 72% (17), the study of Sairam et al. reported 88% (14) and in the study of Zhang et al. 92% (6). These differences are probably due to the studies' inclusion and exclusion criteria, the samples' classification, and the infants' follow-up time.

In our study, the incidence of adverse outcomes after birth in cases of bilateral PHN in the second trimester was almost twice as high as in cases of unilateral PHN at the same time (15.6% vs. 8.3%). Similar to our study, Kim et al. showed that adverse outcomes in bilateral cases were more than unilateral (38% vs. 25%) (18).

In our study, the incidence of adverse outcomes after birth was significantly higher in

unilateral PHN on the left side in the 3rd trimester than on the right side. Consistent with this finding, in Zhang et al.'s study, based on ultrasounds from 20 weeks to 40 weeks of pregnancy, the adverse outcomes in unilateral PHN on the left side were more than right (83% vs. 17%) (6). In many studies, the adverse outcome after birth in these infants was not reported separately for right and left hydronephrosis (15, 16, 19, 20).

Based on our results, the mild form of PHN in the 2nd and 3rd trimesters of pregnancy included almost two-thirds of the cases. As this finding, two other studies reported that a mild form of PHN has been more common (5, 14). According to the findings of this study, the incidence of adverse outcomes after birth in moderate to severe cases of PHN in the 2nd trimester was six times higher than in mild cases. Also, in the 3rd trimester, none of the mild cases had an adverse outcome, but 58.3% of the moderate to severe cases had an adverse outcome. Consistent with our study, Gokaslan et al. stated that the degree of PHN was associated with an increased risk of urologic problems after birth. They reported that

spontaneous recovery in patients with mild PHN was 64% versus 29% in those with severe PHN. (21). Similar findings were also reported by Sen et al. in their study (15).

In a study by Elmaci et al., PHN was divided into two groups of diameter <10 mm and  $\geq$ 10 mm based on the anterior-posterior diameter of the renal pelvis. The rate of complete spontaneous recovery in the first group was 92.7%, and in the second group, it was 51.1% (17). Also, in the study of Loardi et al. (12) with an increase in the average size of the APRPD, the adverse outcome was significantly higher, which was in line with the results of this study.

Regarding the incidence of pregnancy complications, the incidence of adverse outcomes in cases of oligohydramnios was more than twice that of cases with normal amniotic fluid volume (28.6% vs. 11.6%). In Shukla et al.'s study, having oligohydramnios, like the severity of PHN, was a significant predictor for adverse outcomes after birth (16).

In this study, out of 50 fetuses with PHN, 74% were boys and 26% were girls. In line with this finding, there are other studies, such as in the study of Elmaci et al., 78% of boys and 22% of girls (17) and in the study of Zhang et al., 60% of boys and 40% of girls (6) and in the study of Kim et al., 79% of boys and 21% of girls (18) were diagnosed. It seems that the evolution of the urinary system in boys has a role in the higher incidence of PHN. Also, in our study, the incidence of adverse outcomes after birth in boys was twice as high as in girls, which is in line with our study; in Sadeghi et al.'s study, the incidence of adverse outcomes in boys was 2.5 times (22). However, in the study of Kim et al., although the incidence of PHN in boys was four times that of girls, the incidence of adverse outcomes did not differ between the two groups (18). It could be because the severity of PHN was less in boys.

In the present study, bilateral PHN was more common in the 2nd and 3rd trimesters of pregnancy than unilateral, which was in line with the study of Kim et al. (18). However, in some studies, the frequency of unilateral PHN has been mentioned more (5, 23). In Tombesi's study, the most common cause was bilateral PHN in boys, which causes hydroureteronephrosis. In our study, cases with severe PHN accompanied by hydroureteronephrosis were excluded.

Like most other studies, this study found that PHN was continued due to causes such as vesicoureteral reflux and posterior urethral valves (11, 12, 24).

According to the results of this study, the sensitivity and specificity of the anteroposterior diameter of the pelvis of 4 mm in the second trimester to predict the adverse outcome on the right side is 14.57% and 23.26%, and on the left side is 85.7% and 25.58%. The sensitivity and specificity of the anteroposterior diameter of the pelvis is 7 mm in the third trimester for predicting the adverse outcome on the right side, 85.7% and 53.48%, and on the left side, 100% and 65.12%, respectively. In this way, the sensitivity and specificity of the anteroposterior diameter of the pelvis to predict the adverse outcome in the third trimester is higher than in the second trimester. In line with this finding, in the study of Shukla et al., it was also concluded that most of the parameters for diagnosing PHN at 32 weeks of pregnancy have more sensitivity and specificity than at 28 weeks (16). Also, in the study of Kim et al. (2012), it was concluded that the APRPD measured in the 3rd trimester is the most accurate for predicting adverse outcomes after birth (18). In line with this study, in the study of Plevani et al. (2014), the threshold of the APRPD  $\geq$  7 mm in the 3rd trimester has been reported to have a sensitivity of 100% and a specificity of 23% to predict an adverse outcome (25).

The strong point of this study is the prospective and follow-up of affected fetuses after birth. However, because the sampling was done in a convenience sample, the results of the present study may not be generalizable to all fetuses with PHN. If the results are generalized to other fetuses with PHN, it should be done with caution and sufficient knowledge. Another limitation of this study is the limited sample size and follow-up of six months. Therefore, it is suggested that similar prospective studies with a larger sample size and follow-ups up to one year after birth be conducted to obtain more comprehensive results.

## Conclusion

The findings of this study showed that in most cases, the cause of PHN is idiopathic, and spontaneous recovery of hydronephrosis occurs in the fetal period up to six months after birth. Also, the APRPD in the 3rd trimester of pregnancy has better sensitivity and specificity than in the 2nd trimester.

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## Conflicts of interest

The authors declare no competing interests.

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