International Urology and Nephrology (2019) 51:909–915
https://doi.org/10.1007/s11255-019-02138-w

UROLOGY - ORIGINAL PAPER

Prognostic significance of maternal urinary carbohydrate antigen 19-9 for antenatal diagnosis of posterior urethral valve associated with fetal hydronephrosis

Abdol-Mohammad Kajbafzadeh[1] · Shabnam Sabetkish[1] · Nastaran Sabetkish[1]

Received: 25 January 2019 / Accepted: 27 March 2019 / Published online: 6 April 2019

Abstract

Purpose To evaluate the predictive role of maternal urinary CA 19-9 as a non-invasive marker for diagnosing antenatal posterior urethral valve (PUV).

Methods A total of 40 women in the third pregnancy trimester were enrolled. Case group (group A) consisted of 20 women with a diagnosis of antenatal PUV. Twenty women with similar gestational age, fetal sex, normal US, and no history of congenital anomalies were chosen as a control group (group B). Maternal urine samples were collected and urinary CA 19-9 was measured in both groups. The correlations between maternal urinary CA 19-9 and APD (measured during pregnancy and the initial evaluation of the newborn) were assessed. CA 19-9 level in first urine of neonates was also evaluated.

Results The mean ± SD of maternal urine CA 19-9 was higher in PUV group compared to the control group (131.6 ± 23.8 vs. 13 ± 2.7 U/mL). In addition, there was a significant correlation between maternal urinary CA 19-9 and the APD measured at the third trimester ($p < 0.001$) and the initial evaluation of fetus after birth according to SFU grading system ($p < 0.001$). However, no significant difference was found between gestational age and urinary CA 19-9 level ($p = 0.34$). There was also a significant correlation between the CA 19-9 level in first urine of neonates and CA 19-9 level of maternal urine ($p < 0.001$).

Conclusions This is the first time that maternal urinary CA 19-9 has been applied as a noninvasive and practical diagnostic marker in antenatal PUV.

Keywords Prenatal diagnosis · Hydronephrosis · Biomarkers · Urine · CA 19-9 antigen

Abbreviations

ANH	Antenatal hydronephrosis
APD	Anteroposterior renal pelvic diameter
CA 19-9	Carbohydrate antigen
SFU	Society for Fetal Urology

Introduction

Posterior urethral valve (PUV), as the most frequent cause of pediatric obstructive uropathy, affects 1 out of 5000–8000 male fetuses [1]. PUV has the most destructive consequences by progressing to end-stage renal disease (ESRD) in almost 50% of the affected patients [2, 3]. It is valuable that all clinicians be aware of the importance of prenatal diagnosis of PUV as an important underlying cause of antenatal hydronephrosis (ANH) and take measures to prevent the dissemination of potentially damaging consequences as a result of inappropriate, costly, and invasive therapies.

Numerous systems have been used to diagnose and evaluate the grade of ANH [4]. Although anteroposterior pelvic diameter (APD) is objective for prediction of pathology, other features are also necessary for determining the severity of ANH. In general, the Society of Fetal Urology (SFU) has been considered as the most appropriate grading criteria for the diagnosis and grading of ANH [5]. It is well described that infants diagnosed as obstructive nephropathy along with SFU grades III and IV should be carefully monitored with serial ultrasonography (US) [6]. Having in mind the pitfalls of conventional imaging, renal US, differential radionuclide renal scans, and urinary creatinine concentration in making an accurate decision in diagnosis and management of PUV and severe ANH [7], finding a cost-effective and

✉ Abdol-Mohammad Kajbafzadeh
kajbafzd@sina.tums.ac.ir

[1] Pediatric Urology and Regenerative Medicine Research Center, Section of Tissue Engineering and Stem Cells Therapy, Children's Hospital Medical Center, Tehran University of Medical Sciences, Tehran, Iran

non-invasive substitute is crucial for accurate diagnosis of severe PUV in cases who are in need of urgent surgical procedure.

The identification of prenatal biomarkers that predict postnatal outcomes of the affected fetus is the main research goal. It has been reported that CA 19-9 which is slightly expressed in the normal renal pelvis may reach higher levels in some cases with severe hydronephrosis [8, 9]. In this context, we have recently found a significant relationship between maternal urinary Ca 19-9 levels and ANH in a pilot study [10]. The aim of the current study was to focus on the urinary levels of CA 19-9 in pregnant women with a diagnosis of antenatal PUV and compare the results with normal pregnancies. CA 19-9 level in first urine of neonates was also compared in normal patients and those affected with PUV.

Patients and methods

A total of 40 pregnant women in their third pregnancy trimester were enrolled in this study and followed up for diagnosis of PUV between 2014 and 2016 at the department of urology at our institution. The current study was approved by the institutional review board and after explaining the purpose of the study, informed consent was obtained from all pregnant women. Complete history and data collection included maternal age, gestational age (GA), abdominal US, and the presence of comorbidities. Patients with a history of any maternal disease, unintentional abortion/miscarriage, malignancy, the presence of benign disease that could possibly cause an increase in CA 19-9 level, and fetal anomaly (except PUV for case group) were excluded from the study. The study design is summarized in Fig. 1.

Twenty women with a diagnosis of PUV were considered as case group (group A), while women with similar gestational age (GA), normal US, and no history of any congenital anomalies were chosen as a control group (group B). Maternal urine samples were collected and the level of urinary CA 19-9 was measured using an electrochemiluminescence enzyme immunometric kit (Roche Elecsys Kits, Roche Diagnostics GmbH, Mannheim, Germany).

Hydronephrosis grade was evaluated according to the APD measured at the third trimester, and the SFU grading system in the initial evaluation of fetus after birth ("Appendix") [11]. No hydronephrosis was categorized by SFU grade = 0 and an APD diameter ≤ 7 mm, mild hydronephrosis was categorized by SFU grade I–II and an APD of 7–10 mm, moderate hydronephrosis was categorized by SFU

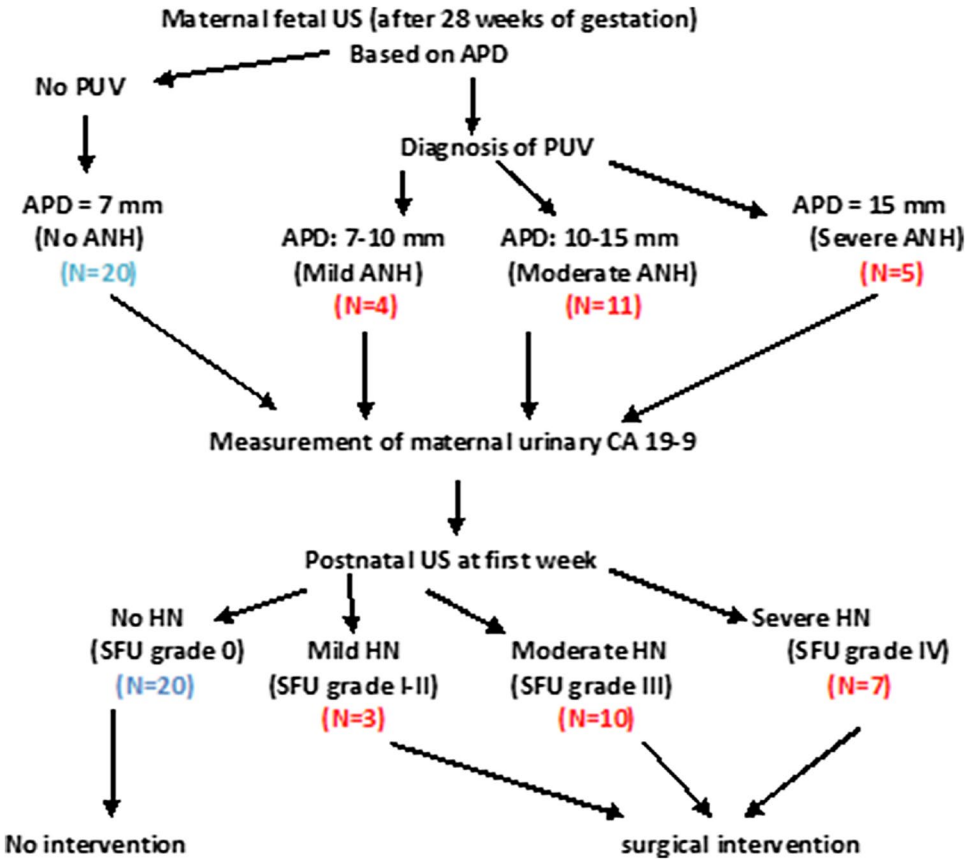

Fig. 1 Diagnostic algorithm for managing ANH. *SFU* indicates Society of Fetal Urology, *US* ultrasonography

grade III and an APD of 10–15 mm, and severe hydronephrosis was defined as SFU grade IV and an APD ≥ 15 mm.

In addition, the correlations between maternal urinary CA 19-9 levels and the APD measured at the third trimester and the initial evaluation of fetus after birth were assessed with abdominal ultrasound (between 3 and 4 days of life, according to SFU grading system); CA 19-9 levels in first urine of neonates were also measured to evaluate the correlation between CA 19-9 level in first urine of neonates and CA 19-9 level of maternal urine.

Results

The prenatal and postnatal characteristics of fetuses in the control group and different types of hydronephrosis in case group are summarized in Table 1. The mean ± SD of maternal age was 28.7 ± 1.8 and 29.4 ± 2.1 years in group A and B, respectively. The mean ± SD of GA was 31.24 ± 0.1.8 and 29.58 ± 2.1 weeks at the time of collecting maternal urinary samples in groups A and B, respectively.

According to the results of prenatal US, 4 fetuses had mild AHN (APD: 8.53 ± 0.24 mm); while 11 and 5 fetuses suffered from moderate and severe AHN (13.33 ± 0.33 and 19 ± 0.58 mm, respectively). In addition, the APD of controls was 5.46 ± 0.1 mm. Postnatal US was performed according to SFU grading, the results of which were quite similar to the prenatal evaluation with a low increase in hydronephrosis grade from the prenatal period to postnatal time. Accordingly, three fetuses had grade II, while ten and seven fetuses suffered from grade III and IV. In addition, all the neonates of the control group were in grade 0 of hydronephrosis according to SFU grading.

The respective mean ± SD maternal urinary CA 19-9 level in control and PUV group was 131.6 ± 23.8 and 13 ± 2.7 U/mL. The mean ± SEM neonatal urinary CA 19-9 level in each group was as follows: 14.59 ± 3.07 U/mL in the control group, and 331.62 ± 33.85 U/mL in PUV group. Creatinine level was significantly lower in the control group in the third postnatal day, compared with that of PUV group (0.6 ± 0.2 vs. 1.7 ± 0.3 mg/dL, $p = 0.03$).

The correlation between maternal urinary CA 19-9 and the APD measured at the third trimester was found to be significant ($r = 0.838$, $p < 0.001$). Additionally, a significant correlation was detected between maternal urinary CA 19-9 and the initial evaluation of fetus after birth according to SFU grading system ($r = 949$, $p < 0.001$). Statistical analysis revealed a significant correlation between the CA 19-9 level in first urine of neonates and CA 19-9 level of maternal urine ($r = 0.990$, $p < 0.001$). However, we found no significant correlation between gestational age and urinary CA 19-9 level ($p = 0.34$) or maternal age and urinary CA 19-9 level ($p = 0.45$) (Table 1, Fig. 2).

Bladder outlet obstruction was relieved in all cases with PUV; using a urethral catheter, and when the child was stable, cystoscopic valve ablation or vesicostomy was performed.

Table 1 Comparison of study variables in PUV and control groups

	PUV group ($N = 20$) Mean ± SD (range)	Controls ($N = 20$) Mean ± SD (range)	p value
Maternal age (years)	28.7 ± 1.8 (26–32)	29.4 ± 2.1 (28–35)	0.82
GA (weeks)	31.24 ± 1.8 (28–37)	29.58 ± 2.1 (26–35)	0.75
Maternal urinary CA 19-9 (U/mL)	131.6 ± 23.8	13 ± 2.7	0.0001
First urinary CA 19-9 (U/mL)	331.62 ± 33.85	14.59 ± 3.07	0.0001
Creatinine level at day 3 (mg/dL)	Mild ANH: 0.7 ± 0.1 Moderate ANH: 1.9 ± 0.2 Severe ANH: 2.5 ± 0.2	0.6 ± 0.2	0.9 0.003 0.0001
SFU grade	Grade II ($N = 3$) Grade III ($N = 10$) Grade IV ($N = 7$)	Grade 0	
APD measured at the third trimester (mm)	Mild ANH: 8.53 ± 0.24 ($N = 4$) Moderate ANH: 13.33 ± 0.33 ($N = 11$) Severe ANH: 19 ± 0.58 ($N = 5$)	5.46 ± 0.1 ($N = 20$)	

APD ≥ 15 in third trimester was defined as severe ANH

The correlation between maternal urinary CA 19-9 and APD ($p = 0.02$), SFU grading ($p < 0.001$), and first urinary CA 19-9 ($p = 0.03$) was found to be significant

PUV posterior urethral valve, *CA 19-9* carbohydrate antigen 19-9, *GA* gestational age, *SD* standard deviation

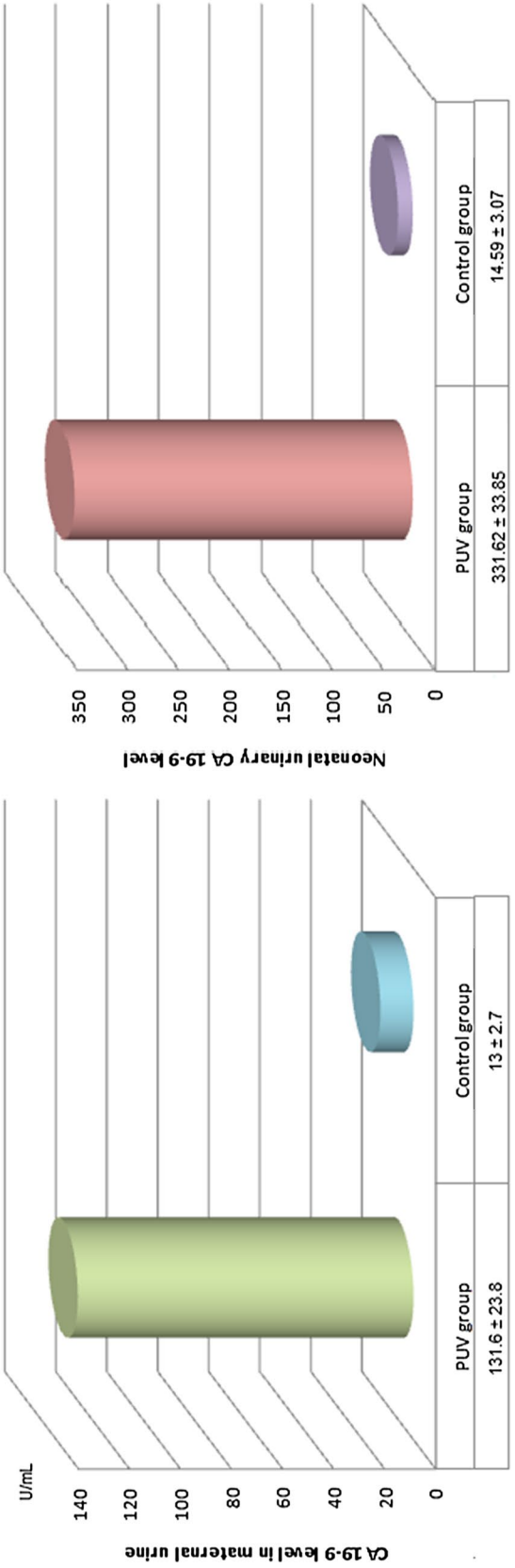

Fig. 2 Correlation between maternal urinary CA-19-9 and APD, SFU, and the first neonatal urinary CA 19-9

Discussion

To the best of our knowledge, this study demonstrated the first published attempt to elucidate increased maternal urinary CA 19-9 levels as a noninvasive diagnostic and predictive biomarker with significant correlation in pregnant women with fetal PUV. There was also a significant correlation between the CA 19-9 level in first urine of neonates with CA 19-9 level of maternal urine. The obtained results could help us to decrease radiation exposure in fetuses by applying non-invasive modalities as the wise alternates and obtaining a more comprehensive prenatal judgment for patients with clinically significant PUV.

Multiple causes such as renal parenchyma dysplasia due to high hydrostatic pressure in the urinary tract [12] and activated vasoactive factors and cytokines in response to obstruction [13] may cause ESRD in patients with PUV. Management of fetuses with PUV will impact the health of the infant after birth which culminates in the more effective postnatal evaluation, timely referral to a pediatric urologist, and promising intervention to reduce damaging outcomes.

Bedsides, US is an efficient tool for exclusion of obstruction in the presence of infection or renal failure and it has been considered to help decision making even for trainee urologists [14, 15]. Postnatal US should be performed for all patients with ANH and the optimal time for US has been considered after the first 48 h of life [16, 17]. So, in the current study, the initial postnatal US was performed within 72–96 h after birth in all patients. However, classifications based only on APD cannot be reliable due to the fact that pyeloectasia without calyx dilatation is usually not a sign of considerable obstruction [18]. The SFU introduced a subjective grading system to study the postnatal evolution of prenatally detected hydronephrosis and classify hydronephrosis [19]. This method of grading has important implications in patient diagnosis, treatment, and outcome. This grading system is frequently used to standardize the severity of hydronephrosis, and compare results among patients and centers. Due to the fact that SFU grading system is regularly used to standardize methods of performing and grading the US and radionuclide examinations in patients with hydronephrosis, we used this system for all children and compared results among patients.

Non-invasive, simple, particular and economic methods such as measuring the urinary biomarkers may be used as an adjunct to radiologic evaluation to increase the sensitivity and specificity of prenatal diagnoses. Although CA 19-9 is known as a tumor marker, later evidence has emerged in support of a role for CA 19-9 elevation in a non-fatal condition such as benign hydronephrosis [20,

21]. In our previous report, we elucidated the association of urinary and cystic fluid levels of tumor marker CA 19-9 and unilateral multicystic dysplastic kidney indicating the significance of this marker in malignant conditions [22]. In one study in 2015, it has been suggested that a high level of urinary CA 19-9 can be considered as a feasible clinically marker for differentiating between obstruction and non-obstructive dilatation [23]. In another study, the results of immunohistochemical (IHC) evaluation confirmed that CA 19-9 was positive in the apical surface of cells in the noncancerous renal pelvic epithelium with hydronephrosis [24]. According to the study of Arik et al., CA 19-9 was found to be elevated in patients with renal failure [25]. Therefore, benign hydronephrosis caused by obstructive dilatation and malignant conditions such as unilateral multicystic dysplastic kidneys is among the differential diagnosis of elevated CA 19-9 level.

Urinary CA 19-9 is a probable biomarker of disease progression and close monitoring of the levels should be taken into consideration for determination of a useful therapeutic manipulation. The prognostic value of this marker has been also evaluated in benign urological diseases such as hydronephrosis and ureteropelvic junction obstruction (UPJO) [8, 22]. In our previous study, we demonstrated that the decrease in urinary CA 19-9 after pyeloplasty in patients with UPJO is considered as effective surgical outcomes and resolution of renal damage [26]. We also demonstrated that the level of CA 19-9 measured in voided urine can be an alternative test with more reliable clinical implications as compared with serum CA 19-9 in patients with UPJO.

It has been recently demonstrated that high urinary CA 19-9 levels can be considered as a non-invasive clinical marker for postnatal differentiation between obstruction and non-obstructive hydronephrosis in patients with unilateral ANH [26]. We used maternal urine CA-19-9 as a noninvasive, clinically applicable marker for diagnosis of PUV with significant correlation with prenatal APD, postnatal SFU grading system and CA 19-9 levels in first urine of neonates.

In spite of the fact that Kutlu et al. did not find a significant correlation between CA 19-9 level and hydronephrosis [27], these values were significantly correlated to one another in our previous study [10]. It has been also supposed that the CA 19-9 level cannot be considered as an efficient parameter for non-invasive prediction of urinary obstruction [27]. Nevertheless, we demonstrated the role of maternal urinary CA 19-9 in terms of diagnosing PUV in our prenatal assessments in which a significant correlation was also found between maternal urinary CA 19-9 and the level of this biomarker in first urine of neonates affected with PUV.

According to our unpublished data, we verified that CA 19-9 in the aspirated amniotic fluid and fetal bladder urine puncture is clinically applicable in patients with congenital obstructive nephropathy (PUV). However, no attempt at prenatal uro-amniotic shunting should be made when the noticeable outcome is predicted by measuring the maternal urinary CA 19-9 [28]. So, due to the invasiveness of this procedure, in the current study, we tried a non-invasive procedure for the more accurate diagnosis of PUV. In another study in 2006, it has been indicated that urinary CA 19-9 can be used as a more efficient method compared to serum CA 19-9 in patients with benign hydronephrosis [20]. The results of the current study suggested maternal urinary CA 19-9 as a noninvasive marker and surrogate for the appropriate follow-up and treatment of patients with PUV.

Atar et al. reported a non-significant association between age and urinary CA 19-9 levels in ANH [23]. Similarly, we demonstrated that CA 19-9 level in maternal urine is a beneficial criterion in evaluating patients with PUV and may increase sensitivity and specificity in obstructive nephropathy detection, while no significant correlation was found between maternal urinary CA 19-9 levels with GA or maternal age.

It has been also demonstrated that patients with PUV had increased levels of CA 19-9 in the amniotic fluid and first urine [29]. Remarkably, the present clinical study represented a different pattern compared to the previous study; it is the first study of measuring the urine levels of CA 19-9 in pregnant women for the diagnosis of fetal PUV.

PUV as a severe congenital abnormality can disturb the development of the urinary tract and decrease the renal function. Therefore, in cases with bilateral renal impairment on prenatal ultrasonography or those with oligohydramnios accompanied by elevated maternal Ca 19-9 level, the diagnosis of PUV is highly suspected. So, the application of this non-invasive, uncomplicated, and cheap method may help the clinicians to be prepared for instantaneous postnatal action to decrease the morbidity rate. In spite of all promising findings of the current study, an absolute need of further studies and evaluating different criteria necessities to avoid serial diuretic renal scintigraphy as a gold standard modality in discriminating obstructive from non-obstructive uropathies in newborns with ANH history. In addition, larger populations and further investigations are needed to elucidate in more detail the correlation of urine CA 19-9 with PUV, plan for further surgical intervention, and allow prediction of long-term renal functional status.

Conclusion

The results of the current study demonstrated that increasing urine CA 19-9 levels in maternal urine is one of the most clinically significant parameters in pregnant women caring fetuses with PUV. In addition, the degree of elevation correlated with some clinical features, such as APD and SFU grade. However, further accumulation of clinical data should

be conducted to draw a firm conclusion regarding the practical implication of the results for the diagnosis of PUV.

Funding None of the authors has direct or indirect commercial financial incentive associating with publishing the article.

Compliance with ethical standards

Conflict of interest None of the authors has direct or indirect commercial financial incentive associated with publishing the article and does not have any conflict of interest, and will sign the Disclosing Form.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

Appendix: SFU grading description

Grade	Description
Grade 0	No dilatation of the renal pelvis
Grade I	Mild dilatation of the renal pelvis (without dilatation of the calyces)
Grade II	Mild dilatation of the renal pelvis and calyces without parenchymal atrophy
Grade III	Moderate dilatation of the renal pelvis and calyces with mild cortical thinning
Grade IV	Gross dilatation of the renal pelvis and calyces plus thinning of the renal parenchyma

References

1. Brown T, Mandell J, Lebowitz RL (1987) Neonatal hydronephrosis in the era of sonography. AJR Am J Roentgenol 148(5):959–963. https://doi.org/10.2214/ajr.148.5.959
2. DeFoor W, Clark C, Jackson E, Reddy P, Minevich E, Sheldon C (2008) Risk factors for end stage renal disease in children with posterior urethral valves. J Urol 180(4 Suppl):1705–1708. https://doi.org/10.1016/j.juro.2008.03.090 **(discussion 1708)**
3. Sarhan O, Zaccaria I, Macher MA, Muller F, Vuillard E, Delezoide AL, Sebag G, Oury JF, Aigrain Y, El-Ghoneimi A (2008) Long-term outcome of prenatally detected posterior urethral valves: single center study of 65 cases managed by primary valve ablation. J Urol 179(1):307–312. https://doi.org/10.1016/j.juro.2007.08.160 **(discussion 312–303)**
4. Sidhu G, Beyene J, Rosenblum ND (2006) Outcome of isolated antenatal hydronephrosis: a systematic review and meta-analysis. Pediatr Nephrol 21(2):218–224
5. Nguyen HT, Herndon CA, Cooper C, Gatti J, Kirsch A, Kokorowski P, Lee R, Perez-Brayfield M, Metcalfe P, Yerkes E (2010) The Society for Fetal Urology consensus statement on the evaluation and management of antenatal hydronephrosis. J Pediatr Urol 6(3):212–231
6. Sinha A, Bagga A, Krishna A, Bajpai M, Srinivas M, Uppal R, Agarwal I (2013) Revised guidelines on management of antenatal hydronephrosis. Indian J Nephrol 23(2):83–97. https://doi.org/10.4103/0971-4065.109403
7. Noyan A, Parmaksiz G, Dursun H, Ezer SS, Anarat R, Cengiz N (2015) Urinary NGAL, KIM-1 and L-FABP concentrations in antenatal hydronephrosis. J Pediatr Urol 11(5):249. e241–249. e246
8. Suzuki K, Muraishi O, Tokue A (2002) The correlation of serum carbohydrate antigen 19-9 with benign hydronephrosis. J Urol 167(1):16–20
9. Ohshio G, Ogawa K, Kudo H, Yamabe H, Higuchi K, Nakashima Y, Manabe T, Tobe T (1990) Immunohistochemical distribution of CA 19-9 in normal and tumor tissues of the kidney. Urol Int 45(1):1–3
10. Kajbafzadeh AM, Keihani S, Kameli SM, Hojjat A (2017) Maternal urinary carbohydrate antigen 19-9 as a novel biomarker for evaluating fetal hydronephrosis: a pilot study. Urol 101:90–93. https://doi.org/10.1016/j.urology.2016.10.038
11. Bhadoo D, Bajpai M, Abid A, Sukanya G, Agarwala S, Srinivas M, Deka D, Agarwal N, Agarwal R, Kumar R (2015) Study of prognostic significance of antenatal ultrasonography and renin angiotensin system activation in predicting disease severity in posterior urethral valves. J Indian Assoc Pediatr Surg 20(2):63–67. https://doi.org/10.4103/0971-9261.151546
12. Lopez Pereira P, Martinez Urrutia MJ, Espinosa L, Jaureguizar E (2013) Long-term consequences of posterior urethral valves. J Pediatr Urol 9(5):590–596. https://doi.org/10.1016/j.jpurol.2013.06.007
13. Simoes e Silva AC, Valerio FC, Vasconcelos MA, Miranda DM, Oliveira EA (2013) Interactions between cytokines, congenital anomalies of kidney and urinary tract and chronic kidney disease. Clin Dev Immunol 2013:597920. https://doi.org/10.1155/2013/597920
14. Surange RS, Jeygopal NS, Chowdhury SD, Sharma NK (2001) Bedside ultrasound: a useful tool for the on-call urologist? Int Urol Nephrol 32(4):591–596
15. Vemulakonda V, Wilcox D, Torok M, Hou A, Campbell J, Kempe A (2015) Inter-rater reliability of postnatal ultrasound interpretation in infants with congenital hydronephrosis. Int Urol Nephrol 47(9):1457–1461
16. Assadi F, Schloemer N (2012) Simplified diagnostic algorithm for evaluation of neonates with prenatally detected hydronephrosis. Iran J Kidney Dis 6(4):284
17. Docimo SG, Silver RI (1997) Renal ultrasonography in newborns with prenatally detected hydronephrosis: why wait? J Urol 157(4):1387–1389
18. González R, Schimke CM (2001) Urteropelvic junction obstruction in infants and children. Pediatr Clin N Am 48(6):1505–1518
19. Rickard M, Easterbrook B, Kim S, Farrokhyar F, Stein N, Arora S, Belostotsky V, DeMaria J, Lorenzo AJ, Braga LH (2017) Six of one, half a dozen of the other: a measure of multidisciplinary inter/intra-rater reliability of the society for fetal urology and urinary tract dilation grading systems for hydronephrosis. J Pediatr Urol 13(1):80 e81–80 e85. https://doi.org/10.1016/j.jpurol.2016.09.005

20. Aybek H, Aybek Z, Sinik Z, Demir S, Sancak B, Tuncay L (2006) Elevation of serum and urinary carbohydrate antigen 19-9 in benign hydronephrosis. Int J Urol 13(11):1380–1384
21. Suzuki K (2007) Elevation of serum and urinary carbohydrate antigen 19-9 in benign hydronephrosis. Int J Urol 14(7):668–669
22. Khorramirouz R, Ebadi M, Rahimi Sherbaf F, Kajbafzadeh A-M (2014) Persistent high level of urinary tumor marker carbohydrate antigen 19–9 in prenatally diagnosed dysplastic kidney. Case Rep Urol 2014:259870
23. Atar A, Oktar T, Kucukgergin C, Kalelioglu I, Seckin S, Ander H, Ziylan O, Kadioglu TC (2015) The roles of serum and urinary carbohydrate antigen 19-9 in the management of patients with antenatal hydronephrosis. J Pediatr Urol 11(3):133. e131–133. e135
24. Suzuki K (2000) Renal pelvic and ureteral cancer with extremely high serum level of carbohydrate antigen 19-9 (CA 19-9): a case report. Nishi Nihon J Urol 62(12):659–663
25. Arik N, Adam B, Akpolat T, Hasil K, Tabak S (1996) Serum tumour markers in renal failure. Int Urol Nephrol 28(4):601–604
26. Kajbafzadeh A-M, Elmi A, Talab SS, Emami H, Esfahani SA, Saeedi P (2010) Urinary and serum carbohydrate antigen 19-9 as a biomarker in ureteropelvic junction obstruction in children. J Urol 183(6):2353–2360
27. Kutlu O, Celik O, Koksal I, Yigit S, Danisman A (2012) Serum carbohydrate antigen 19-9 levels in patients with unilateral hydronephrosis due to urinary lithiasis. Minerva Urol Nefrol 64(3):217–221
28. Muller F, Dommergues M, Mandelbrot L, Aubry M-C, Nihoul-Fekete C, Dumez Y (1993) Fetal urinary biochemistry predicts postnatal renal function in children with bilateral obstructive uropathies. Obstetr Gynecol 82(5):813–820
29. Kajbafzadeh A, Elmi A, Talab SS, Tourchi A, Abdaresfahani S (2010) Fetal urinary new biomarker for prediction of renal and pulmonary function in posterior urethral valves. J Pediatr Urol 6:S46–S47