November 2018

Spectrum, management and outcomes of structural and functional uropathies in children attending a tertiary care center in Karachi; Pakistan

Arshalooz Rahman
Aga Khan University, arshalooz.rahman@aku.edu

Saima Hanif
Aga Khan University

Noor Ul-Ain Baloch
Aga Khan University

Abdul Rehman
Hamad Medical Corporation

Tauqeer Sheikh
Jinnah Medical & Dental College

See next page for additional authors

Authors
Arshalooz Rahman, Saima Hanif, Noor Ul-Ain Baloch, Abdul Rehman, Tauqeer Sheikh, and Mohammad Irfan Ladhani

SHORT REPORT

Spectrum, management and outcomes of structural and functional uropathies in children attending a tertiary care center in Karachi; Pakistan

Arshalooz Jamila Rahman,[1] Saima Hanif,[2] Noor Ul-Ain Baloch,[3] Abdul Rehman,[4] Tauqeer Sheikh,[5] Mohammad Irfan Ladhani[6]

Abstract

Causes and outcomes of children diagnosed with hydronephrosis in resource-limited countries with a low utilization of antenatal ultrasonography remain unexplored. We performed a retrospective, cross-sectional study of all paediatric patients diagnosed with hydronephrosis and managed at a tertiary care center in Karachi, Pakistan between 2005 and 2010. Data relating to demographics, clinical features, etiologies and treatment modalities were systematically collected. Of a total of 234 cases (74.4% male), 83 (35.5%) and 42 (17.9%) were neonates and infants respectively. Congenital urinary tract pathologies were noted in 192(72.2%) patients, of which only 96(50%) had undergone foetal ultrasonography and 77(40.1%) first presented after the age of 1 year. At a median follow-up of 4 years, 24(12.5%) of these patients had evidence of renal dysfunction. Worse urologic outcomes in this study were most likely attributable to delayed diagnosis of congenital urinary tract abnormalities.

Keywords: Hydronephrosis, Urogenital Abnormalities, Prenatal Ultrasonography, Developing Countries

Introduction

Hydronephrosis, a dilatation of the pelvicalyceal system of the kidney, is not a disorder in itself, but, it is a manifestation of congenital or acquired urinary tract obstruction.[1] Hydronephrosis is estimated to affect 1-4.5% of all pregnancies, albeit its significance and optimal management remains controversial.[2]A wide range of disorders can account for hydronephrosis in children, such as ureteropelvic junction obstruction (UPJO), vesicoureteral reflux (VUR), posterior urethral valves (PUV) and other pathologies. Due to widespread utilization of antenatal ultrasonography, most cases of neonatal and infantile hydronephrosis are diagnosed prenatally in resource-rich countries.[3] However, in many low to middle-income countries (LMIC), diagnosis is delayed in such cases as third-trimester ultrasonography is not widely utilized and children present late in the course of their disease.

Utilization of antenatal care services in Pakistan is limited to a mere 33% of the total population.[4] In such settings, the spectrum of children presenting with hydronephrosis and their optimal management differs from those of settings where third-trimester ultrasonography is widely utilized. For instance, guidelines for radiologic evaluation of children with hydronephrosis, VUR or urinary tract infections (UTI) were based on data reported from developed countries and their applicability to low-income countries remains uncertain.[5]

We hypothesized that the causes and outcome of children with hydronephrosis at our tertiary care center may be different from those reported in the published literature. In order to test this hypothesis, we performed a retrospective review of all children diagnosed and managed for hydronephrosis at our institution.

Methods and Results

Our hospital is a tertiary care center located in the city of Karachi-the world's tenth largest urban conglomeration-with an estimated population of over 23.5 million. We performed a retrospective, cross-sectional study using the institutional medical records database. All files with an ICD-9-CM (International Classification of Diseases, 9th Revision-Clinical Modification) code for "hydronephrosis" were retrieved. Patients diagnosed with hydronephrosis between 2005 and 2010 were included, while patients above the age of 16 years were excluded from the study. Using a pre-designed, structured pro forma, data relating to demographics, clinical features, laboratory and radiologic findings, treatment modalities and follow-up visits were systematically collected. Frequencies were calculated for qualitative variables, while mean (standard deviation

[1]Department of Pediatrics, Aga Khan University, Karachi; [2,3]Medical College, Aga Khan University, Karachi; [4]Internal Medicine Section, Department of Medicine, Hamad Medical Corporation, Doha, Qatar; [5,6]Jinnah Medical & Dental College, Karachi

Correspondence: Noor Ul-Ain Baloch e-mail: .noor2000_2004@hotmail.com

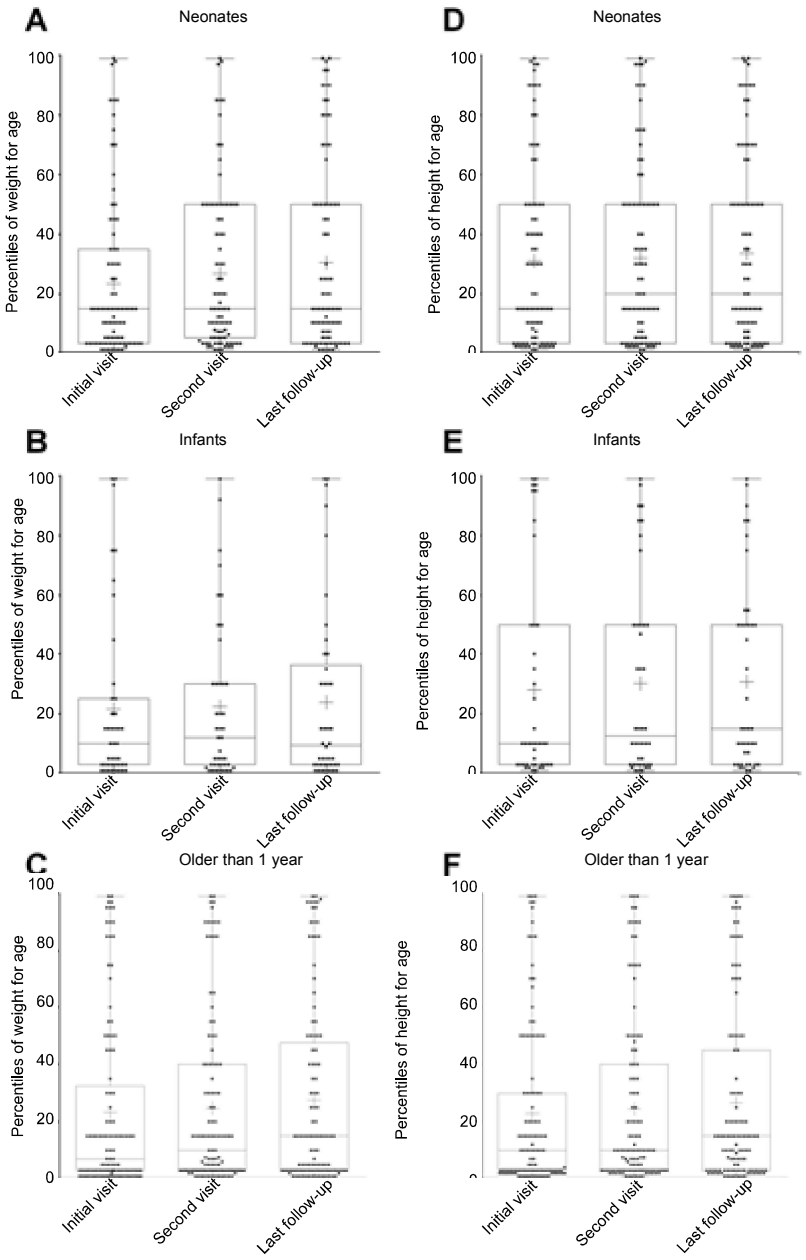

Figure-1: Graph depicting the percentile values of weight (A, B, C) and height-for-age (D, E, F) of study subjects of different ages as measured on first, second and last follow-up visits. Boxes show median and interquartile ranges, plus (+) symbols represent means and lines with bars depict minimum and maximum values.

[SD]) or median (inter-quartile range [IQR]) were computed for quantitative variables. Failure to thrive was defined as a Z-score of less than -2 for weight and height-for-age using the World Health Organization's (WHO) growth charts. Renal dysfunction was indicated by a serum creatinine level of 1.5 mg/dl or more. Retarded growth was defined as a 2-point drop in Z-score for weight or height-for-age on a follow-up visit. Pyuria and haematuria were defined as leukocytes of more than 10 per low power field and erythrocytes of more than 5 per low power field on urine microscopy. Urine culture results were only recorded if the urine specimen was obtained by catheterization, suprapubic aspiration, or cleanly catching a mid-stream sample. Statistical Package for Social Sciences (SPSS) version 20.0 was used for performing statistical analysis.

A total of 234 cases of paediatric hydronephrosis were diagnosed and/or managed at our center between January, 2005 and December, 2010. Of these, 83 (35.5%) and 42 (17.9%) were neonates and infants (at the time of diagnosis) respectively. Boys constituted the bulk of the sample (n=174, 74.4%). Most patients (n=215, 91.9%) were bearing the cost of medical management out-of-pocket. Foetal ultrasonographic scans were performed for 147 (62.8%) children. A substantial proportion of children were diagnosed with hydronephrosis incidentally (n=141, 60.3%). Among symptomatic children, the most common symptoms were fever (n=61, 26.1%), dysuria (n=21, 9.0%), flank pain (n=19, 8.1%) and haematuria (n=12, 5.1%). The median age at presentation was 9.5 (IQR: 0-62) months. The most common causes of hydronephrosis were UPJO (n=77, 32.9%), primary VUR (n=32, 13.7%), PUV (n=29, 12.4%) and calculi (n=29, 12.4%). On presentation, 24(10.3%) and 28(12%) had failure to thrive and renal dysfunction respectively. Moreover, retarded growth was noted in 43 (18.4%) children. Fig. 1 depicts the weight and height-for-age of study subjects at presentation and last follow-up. Initial urinalysis revealed pyuria and haematuria in 50(21.4%) and 43(18.4%) of children respectively. Urine culture obtained at presentation showed growth of pathogenic bacteria in a substantial proportion of children (n=72, 30.8%) with the most common organisms being Escherichia coli (n=23), Klebsiella spp. (n=14), Pseudomonas spp. (n=12) and Enterococcus spp. (n=7). Long-term prophylactic

Table-1: Characteristics of children with hydronephrosis secondary to congenital urinary tract abnormalities.

Characteristics	Subjects with congenital urinary tract abnormalities (n=192)
Sex	
Male	149 (77.6%)
Female	43 (22.4%)
Age (median [IQR])	4 (0-48) months
Age groups	
Neonates	75 (39.1%)
Infants	39 (20.3%)
Older than 1 year	78 (40.6%)
Paying out-of-pocket	188 (97.9%)
Fetal ultrasonography	
Not performed	96 (50%)
Normal	33 (17.2%)
Pelvicalyceal dilatation	63 (32.8%)
Symptoms at presentation	
None	105 (54.7%)
Fever	49 (25.5%)
Dysuria	17 (8.8%)
Flank pain	10 (5.2%)
Haematuria	6 (3.1%)
Poor urinary stream	9 (4.7%)
Abdominal mass	5 (2.6%)
Urinary retention	3 (1.6%)
Causes of hydronephrosis	
Uretero-pelvic junction obstruction	77 (40.1%)
Primary vesicoureteral reflux	32 (16.7%)
Self-resolving fetal hydronephrosis	30 (15.6%)
Posterior urethral valves	29 (15.1%)
Multiple complex malformations	15 (7.8%)
Other congenital causes	9 (4.7%)
Failure to thrive on presentation	18 (9.4%)
Renal dysfunction on presentation	24 (12.5%)
Retarded growth	32 (16.7%)
Pyuria	46 (24.0%)
Haematuria	28 (14.6%)
Results of urine culture	
No growth	136 (70.8%)
Escherichia coli	18 (9.4%)
Klebsiella spp.	10 (5.2%)
Pseudomonas spp.	10 (5.2%)
Enterococcus spp.	6 (3.1%)
Enterobacter aerogenes	4 (2.1%)
Candida spp.	3 (1.6%)
Staphylococcus aureus	4 (2.1%)
Others	1 (0.5%)
Prophylactic antibiotics	36 (18.7%)
Surgical/interventional procedures	
Anderson-Hynes pyeloplasty	40 (20.8%)
Fulgration of posterior urethral valves	15 (7.8%)
Cystoscopy	12 (6.2%)
Extra-corporeal shock-wave lithotripsy	0 (0%)
Vesicostomy	9 (4.7%)
Percutaneous nephrostomy	4 (2.1%)
Nephrectomy	5 (2.6%)
Pyelolithotomy	0 (0%)
Ureterolithotomy	0 (0%)
Ureteric re-implantation	3 (1.6%)
Other procedures	3 (1.6%)
Duration of follow-up (median [IQR])	4 (2-7) years
Renal dysfunction on follow-up	22 (11.5%)
Failure to thrive on follow-up	14(7.3%)

Continued to next column .....

Table-1, continued from previous column

IQR = Interquartile range.

antibiotics were employed in the management of 42 (17.9%) patients. Surgical or interventional procedures were performed in 123 (52.6%) cases. The most commonly performed procedures included Anderson-Hynes pyeloplasty (n=40), fulgration of PUV (n=15), extracorporeal shock-wave lithotripsy (n=11) and vesicostomy (n=9). Of 102 (43.6%) patients who underwent radionuclide imaging, 37 (15.8%) and 15 (6.4%) had reduced renal functioning and renal cortical scarring respectively. At a median follow-up of 4 (IQR: 1-7) years, 24(12.5%) had evidence of renal dysfunction and another 18(7.7%) had failure to thrive. These results are summarized in Tables 1 and 2.

A substantial proportion of children (n=192, 72.2%) had congenital urinary tract pathologies, of which only 96(50%) had undergone foetal ultrasonography and 63(32.8%) had evidence of antenatal hydronephrosis. The median age at presentation for these children was 4 (IQR: 0-48) months with 77(40.1% first presenting after the age of 1 year. On presentation, 18(9.4%) and 22(11.5%) had failure to thrive and renal dysfunction respectively, while retarded growth was noted in 32(16.7%) of cases. Initial urinalysis revealed pyuria and haematuria in 46(24%) and 28(14.6%) of children respectively. Urine culture obtained at presentation showed growth of pathogenic bacteria in 56(29.2%) of patients. At a median follow-up of 4 (IQR: 2-7) years, 10(5.2%) had evidence of renal dysfunction and another 14(7.3%) had failure to thrive.

In our study cohort, more than half of all patients were aged 1 year or less at the time of diagnosis. As is true of most low-income countries, most patients were uninsured and had to bear the cost of treatment out-of-pocket. Boys constituted for nearly three-fourths of the total sample and this may attributable to the male-

Table-2: Characteristics of children with acquired causes of hydronephrosis

Characteristics	Subjects with acquired structural and functional uropathies (n=42)
Sex	
Male	25 (59.5%)
Female	17 (40.5%)
Age (median [IQR])	24 (1-62) months
Age groups	
Neonates	8 (19.1%)
Infants	3 (7.0%)
Older than 1 year	31 (73.9%)
Paying out-of-pocket	27 (64.3%)
Fetal ultrasonography	
Not performed	9 (21.4%)
Normal	25 (59.5%)
Pelvicalyceal dilatation	8 (19.1%)
Symptoms at presentation	
None	30 (71.4%)
Fever	12 (28.6%)
Dysuria	4 (9.5%)
Flank pain	9 (21.4%)
Haematuria	6 (14.3%)
Poor urinary stream	1 (2.44%)
Causes of hydronephrosis	
Urinary calculi	29 (69.1%)
Secondary vesicoureteral reflux	7 (16.7%)
Other acquired causes	6 (14.3%)
Failure to thrive on presentation	4 (9.5%)
Renal dysfunction on presentation	8 (19.1%)
Retarded growth	11 (26.2%)
Haematuria	15 (35.7%)
Pyuria	4 (9.5%)
Results of urine culture	
No growth	19 (45.3%)
Escherichia coli	5 (11.9%)
Mixed flora	5 (11.9%)
Klebsiella spp.	4 (9.5%)
Pseudomonas spp.	2 (4.8%)
Enterococcus spp.	2 (2.4%)
Enterobacter aerogenes	1 (2.4%)
Candida spp.	1 (2.4%)
Others	3 (7.1%)
Prophylactic antibiotics	6 (14.3%)
Surgical/interventional procedures	
Extra-corporeal shock-wave lithotripsy	11 (26.2%)
Pyelolithotomy	5 (11.9%)
Percutaneous nephrostomy	4 (9.5%)
Ureterolithotomy	4 (9.5%)
Nephrectomy	2 (4.8%)
Duration of follow-up (median [IQR])	2 (1-4) years
Renal dysfunction on follow-up	3 (7.1%)
Failure to thrive on follow-up	1 (2.4%)

dominated nature of the local society. Utilization of antenatal ultrasonography in our study subjects was 147(62.8%), which was higher than the previously quoted figure of 33% for Pakistan.[4] This may be reflective of the fact that our tertiary care center caters to the health-care needs of the urban population of Karachi, while more than half of the country's population resides in rural areas. The etiologies of hydronephrosis noted in our study were comparable to those reported in previously published series.[6,7] However, 77(40.1%) of patients with congenital urinary tract anomalies were diagnosed after the age of one year, which was in stark contrast with reports published from centers in developed nations.[6-8] Moreover, a substantial proportion of patients had retarded growth 43(18.4%) and poor weight gain and/or evidence of renal dysfunction at long term follow-up 24(12.5%). Abundant evidence has shown that urologic outcomes in children with congenital urinary tract anomalies (such as PUV) can be improved by timely diagnosis.[3,9] Moreover, development of VUR, renal scarring and end-stage renal disease has been associated with the presence of congenital urinary tract malformations and renal hypodysplasia.[1,10] As such, older age at presentation and delayed diagnosis can account for the higher prevalence of renal dysfunction and poor growth observed in our study. Long-term antibiotic prophylaxis was prescribed to 42(17.9%) of our study subjects. Although antibiotic prophylaxis may reduce the incidence of recurrent UTI, its impact on incidence of renal scarring and long-term kidney function remains controversial.[1] Therefore, early diagnosis and correction of surgically amenable urinary tract malformations may theoretically reduce the need for antibiotic prophylaxis.[1,9,10] This in turn has the potential to cut the cost of health-care for patients paying out-of-pocket and reduce the selection of multi-drug resistant organisms.

Conclusions

The results of our study showed that the etiologies of hydronephrosis in our study cohort were similar to those reported from more developed centers of the world. However, a substantial proportion of patients with congenital urinary tract malformations were diagnosed late in the course of their disease, which led to worse overall outcomes. Strategies to detect congenital urinary tract malformations at an earlier age may improve urologic outcomes for children in LMIC and may potentially reduce the overall cost of treatment.

Utilization of antenatal ultrasonography in our study population was not optimal and therefore, targeted interventions to improve utilization of antenatal ultrasonography may allow an earlier diagnosis of congenital urinary tract anomalies.

Disclaimer: None to declare.
Conflict of interest: The authors declare no conflict of interests regarding the findings reported in this study.
Funding disclosure: None to declare.

References

1. Awais M, Rehman A, Baloch NUA, Khan F, Khan N. Evaluation and management of recurrent urinary tract infections in children: state of the art. Expert Rev. Anti Infect Ther. 2015; 13: 209-31.
2. Liu DB, Armstrong WR III, Maizels M. Hydronephrosis: prenatal and postnatal evaluation and management. Clin Perinatol. 2014; 41: 661-78.
3. Shamshirsaz AA, Ravangard SF, Egan JF, Prabulos AM, Shamshirsaz AA, Ferrer FA, et al. Fetal hydronephrosis as a predictor of neonatal urologic outcomes. J Ultrasound Med. 2012; 31: 947-54.
4. Mumtaz Z, Salway SH. Gender, pregnancy and the uptake of antenatal care services in Pakistan. Sociol Health Illn. 2007; 29: 1-26.
5. Awais M, Rehman A, Zaman MU, Nadeem N. Recurrent urinary tract infections in young children: role of DMSA scintigraphy in detecting vesicoureteric reflux. Pediatr Radiol. 2015; 45: 62-8.
6. Chevalier RL, Peters CA. Congenital urinary tract obstruction: Proceedings of the State-Of-The-Art Strategic Planning Workshop-National Institutes of Health, Bethesda, Maryland, USA, 11-12 March 2002. Pediatr Nephrol. 2003; 18: 576-606.
7. Toka HR, Toka O, Hariri A, Nguyen HT. Congenital anomalies of kidney and urinary tract. Semin Nephrol. 2010; 30: 374-86.
8. Lee RS, Cendron M, Kinnamon DD, Nguyen HT. Antenatal hydronephrosis as a predictor of postnatal outcome: a meta-analysis. Pediatrics. 2006; 118:586-93.
9. Kousidis G, Thomas DFM, Morgan H, Haider N, Subramaniam R, Feather S. The long-term outcome of prenatally detected posterior urethral valves: a 10 to 23-year follow-up study. BJU Int. 2008; 102:1020-4.
10. Montini G, Tullus K, Hewitt I. Febrile urinary tract infections in children. N Eng J Med. 2011; 365:239-50.