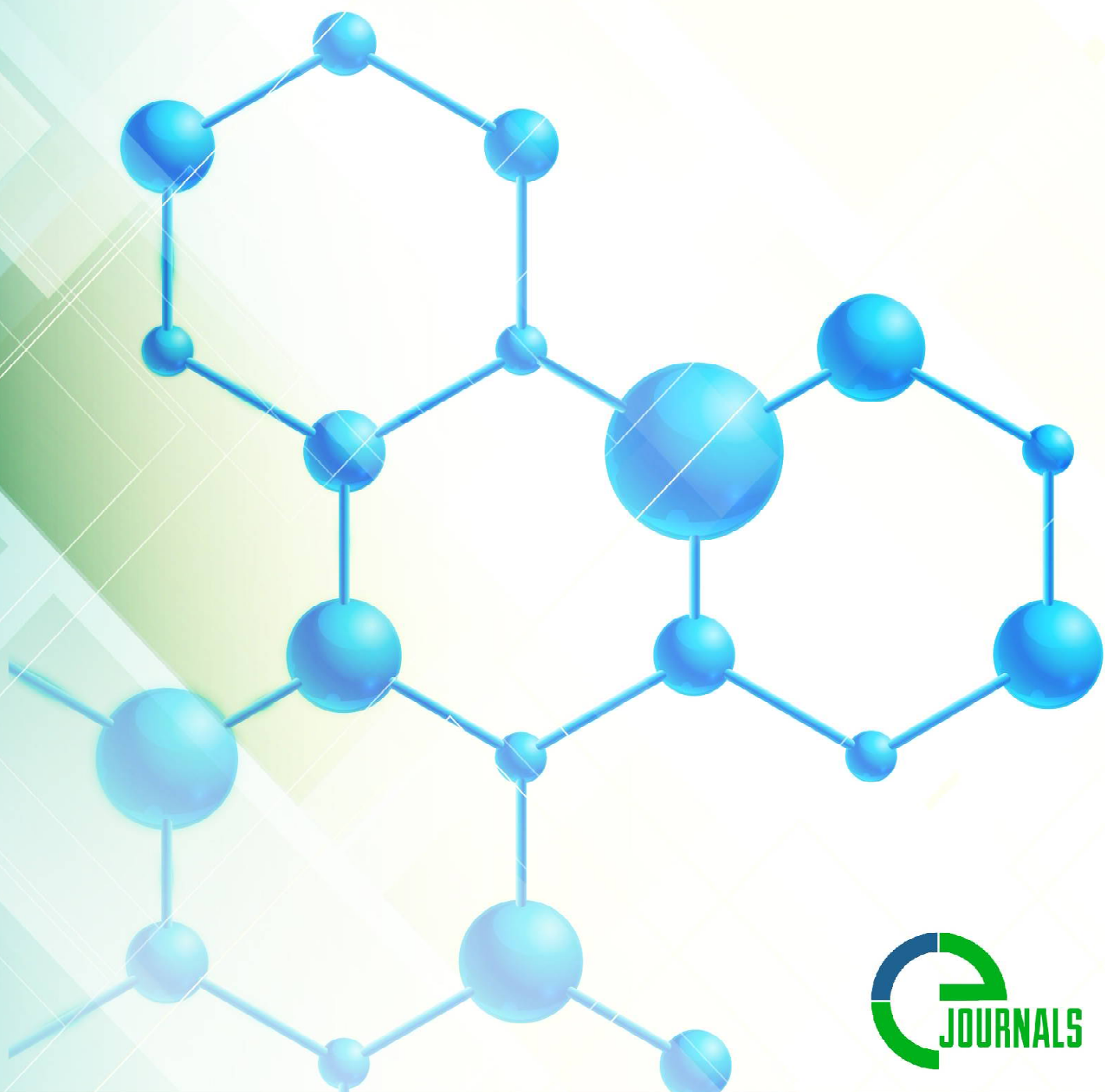


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**IS THE MEGAURETER THE PROBLEM OF YESTERDAY, TODAY OR TOMORROW?****Yu.M. Akhmedov****I.Yu., Akhmedov****G.S. Karimova**

Samarkand State Medical Institute, Republic of Uzbekistan

*Abstract. Congenital malformations of the ureters, in particular the megaureter, are a frequent and fairly common pathology of the urinary system. According to different authors, it makes up from 22% to 40% of all malformations. The increase in the number of early diagnosis of this disease, the lack of a unified view of the factors of their development, the use of various diagnostic methods, the presence of a large number of surgical treatment methods, the high percentage of unsatisfactory results and the prospect of developing new treatment algorithms make this disease an urgent issue of pediatric surgery.*

*Keywords: Megaureter, reflux, obstruction, ureters, anomaly, dysfunction, ureterovesical segment.*

**Introduction.**

Congenital malformations of the ureters, in particular the megaureter, are a frequent and fairly common pathology of the urinary system. According to different authors, it makes up from 22% to 40% of all malformations [2].

Every year in a scientific children's surgical publication there are a fairly large number of works relating to the problem of obstruction of the ureters in children. This is due to the high frequency of development and the increase in the number of early diagnosis of this disease, the lack of a single look at the factors of their development and, as a result, the use of a large number of surgical treatment methods as well as methods of preoperative algorithms for preparing the patient for treatment, as well as the appointment of postoperative care and drug treatment [4].

Among pediatric patients with certain diseases, congenital anomalies of the urinary tract occur in up to 40% of cases. Most often, congenital anomalies of the ureters are diagnosed at the age of several months to 10 years, there are cases of accidental diagnosis in the study for other complaints. Also of great importance is the level of development of diagnostic methods and the general state of medicine in each region [1,19].

The manifestation of congenital anomalies of the ureters in children depends in most cases not on the stage, but on the period of the onset of the disease and the appearance and increase in the number of secondary complications in each patient [12,20].

Despite the annual development of medicine, according to several authors, the megaureter has a tendency to increase the incidence rate, the violation of the urodynamics caused by this pathology creates favorable conditions for the development of an ascending infection (pyelonephritis) and scarring of kidney tissue with a further loss of their function. Even with modern diagnostic systems and already established methods of treating this disease with late diagnosis and inappropriate treatment tactics, 23-27% of children develop one of the most formidable complications of chronic renal failure (CRF) [3,6,13].

In the early diagnosis and an attempt to quickly solve the problems of this disease, unsatisfactory results of surgical treatment are observed in 10-30% of patients, which

gives rise to further research and implementation of the latest achievements of medicine and pharmacology in solving the problem [20].

**Incidence.** Megaureter is a common diagnosis in children visiting a pediatric urologist, accounting for 28% of children with urinary tract obstruction. The diagnosis is more common in boys than in girls, and in most cases is on the left side. It can be bilateral in 25% of cases, and the contralateral kidney is absent or present as dysplastic in 10-15% of cases [11,12,13].

**Embryology and pathophysiology.** Many scientific studies have been carried out describing the histological origin of the megaureter, and although they often differ from each other, all studies often show an abundance of connective tissue in the abnormal ureter [17,18,19]. Lee et al. demonstrated that the ratio of collagen to smooth muscle in normal ureters is 0.52, while in obstructive and reflux megaureters it is 0.78 and 1.99, respectively [21]. Other studies have shown the presence of smooth muscle cells in these ureters that produce abnormally increased amounts of collagen. It has also been proven that the muscles in these segments of the ureter react abnormally to neurotransmitters, emphasizing the abnormal behavior of these cells [17,18,19,20].

Primary obstructive megaureter is considered functional obstruction. It is believed that in the ureter there is an aperistaltic articular (adynamic) segment, which leads to insufficient peristalsis of the ureter and, consequently, to the outflow of urine. This distal segment was examined histologically, and it was found that it contains elevated levels of collagen type I and III (mainly type I). It is this enhanced fibrosis that is associated with a violation of intercellular connections and leads to arrhythmias and ureter obstruction [7,8,9,11]. However, there are many other theories regarding the development of obstructive megaureters. Some scientists have proved atrophy of the internal longitudinal muscles in these segments of the ureter (the longitudinal muscles transmit peristalsis) and hypertrophy of the external, compressive circular muscle, which leads to obstruction [12,13].

Other histological findings that claim to reflect the causal aspect of the obstructive megaureter include distal ureter segments without muscle tissue, but simply a fibrous, static end. At the same time, distal segments of the ureter with a non-urethral, non-destructive muscle, which reacts excessively to the adrenergic stimulus, leading to an almost tonic contraction, have been documented in others [1,14,15,16]. It was found that the proximal enlarged segment of the ureter was also found in the composition of the altered connective tissue, and this fibrosis and the expansion itself can lead to ureter arrhythmias and poor transmission of peristaltic waves. It is important to note that the expansion of the upper parts of the tract (although in itself it represents a significant pathology) plays an important role in the reaction of the urinary tract to the presence of obstruction. The urinary system in children is more flexible than in adult patients, and this expansion allows you to reduce pressure, allowing the kidneys to produce urine in the urinary tract [1,2,3]. In addition to the above-described adynamic segment on the terminal ureter in the obstructive megaureter, other anatomical causes may lead to a similar clinical scenario. Both congenital distal ureteral strictures and distal ureter valves can be almost indistinguishable from the classic obstructive megaureter [17,18,19]. Secondary obstructive megaureter is an obstructive process secondary to increased intravesical pressure of any other cause. Common causes are spinal dysraphism and a neurogenic bladder, which can raise detrusor pressure to more than 40 cm mm of water. Art., causing physiological obstruction and hydronephrosis. Neurogenic urinary dysfunction, if it is severe enough to raise the pressure in the bladder above a safe range, can also be



the cause. Posterior urethral valves or other causes of infravesical obstruction can also lead to similar results [1,18,19]. Other anatomical causes of secondary, distal obstruction of the ureter include ureterocele, ectopic ureter, diverticulum of the bladder, periurethral fibrosis, and external compression of the retroperitoneal tumor, masses, or aberrant vessels [1,18,19].

The primary and secondary reflux megaureter are simply a reflux ureter that is dilated. Pathology mimics the pathology of any reflux ureter with a short intravesical ureter and submucosal tunnel. They may be associated with abnormalities of the ureterovesical segment, which makes reflux more likely, such as periurethral diverticula. In some children, in addition to the ureters, megacystomegaureter syndrome is observed, in which the bladder is noticeably widened and has a thin wall [18]. The distal segment of reflux megaureters also shows a histological disorder with increased fibrosis (very similar to obstructive megaureters); however, in these cases, type III collagen is predominant [11].

Primary non-obstructive non-reflux megaureter - most cases of the megaureter end up being non-obstructive, non-reflux species. This is very encouraging, as it confirms that a simple observation will serve as therapy for most children. However, as already mentioned, the absence of obstruction can be difficult to prove [1,18]. When evaluating a megaureter, some important points should be taken into account that can help prevent unnecessary interference. First of all, the fact that the baby was born with a functioning kidney indicates that any degree of ureteral obstruction is not complete, since the kidney would not form normally under conditions of an early or very high degree of obstruction. The fetus produces large volumes of urine compared to an infant, and if this diuresis precedes the natural canalization of the distal ureter, a megaureter may develop (hypothesis of delayed maturation). Since the ureter in the fetus is very obedient, a slight increase in the flow of urine can cause the ureter to expand even in the absence of obstruction and reflux. It is this compatible urinary system that allows the baby's kidney to continue to function in conditions of varying degrees of obstruction or reflux without suffering injuries under pressure, so expansion may not cause harm to the child [1,2,3,18].

Secondary non-obstructive non-reflux megaureter. Cases of non-obstructive and non-reflux megaurether for a reason not related to the anatomy of the ureter are called secondary. It is in this category that dilatation is possible due to a high yield of fetal urine, increased elasticity of the ureter of the fetus (due to the composition of the extracellular matrix, including increased type II collagen and elastin concentration), or transient obstruction during development (for example, ureteral folds) or delay in the development of normal peristalsis) [18]. There are many other relatively benign causes of the secondary megaureter. For example, urinary tract infections can lead to a temporary expansion of the ureter due to the presence of bacterial endotoxins that can inhibit peristalsis. As already mentioned, any increase in urine output can lead to an expansion of the fetal / baby collection system. Some possible causes of diuresis include lithium toxicity, diabetes insipidus or diabetes mellitus, sickle cell nephropathy, or psychogenic polydipsia [18].

Diagnosics. Currently, the use of prenatal ultrasound has increased the diagnosis of megaureter. Cases detected later in life are often accompanied by urinary tract infections, hematuria and / or pain [21,22]. After diagnosis (in utero or after childbirth), the first and most affordable method is an ultrasound of the kidneys and bladder. Ultrasonography is a simple, safe and painless study that can provide important information about kidney

size, parenchyma thickness, echogenicity and architecture, as well as the expansion of the renal pelvis and ureter, the thickness of the bladder wall and, in some cases, the urethra. Although an experienced pediatric surgeon can conclude some functional diagnoses from ultrasound examinations, it is important to remember that an ultrasound exam is only descriptive and does not provide detailed information about renal function [19,21].

Further, an integral part of the diagnosis of a megaureter is the conduct of radionuclide imaging and excretory urography, which make it possible to assess the structure of the kidneys and ureters, as well as their functional state.

A radionuclide study reveals a decrease in the accumulation and elimination of the radiopharmaceutical by the parenchyma and the collective kidney system. In this case, it is necessary to take into account the dependence on age for removing the radiopharmaceutical in children of the first weeks of life.

Excretory urogram visualize the delay in the discharge of contrast medium by the kidneys, the violation of the collector system, the expansion and tortuosity of the ureters. To conduct this study, a radiopaque substance is administered at a rate of 1-2 mg / kg body weight, but not more than 60 ml per study. Pictures are taken after 1.5.15.30 minutes from the time of administration and after urination. Also, if necessary, you can take delayed pictures after 1, 2 and 3 hours.

For a more accurate diagnosis, a specialist can perform cystoureterography myciation to determine the degree of reflux; a warm solution of an iodine-containing radiopaque compound is introduced into the urinary bladder through an installed catheter until an imperative urge. Pictures are taken with a full bladder during urination and on an empty bladder.

Also, patients can undergo cystoscopy in which it is possible to visualize the signs of chronic cystitis (bullous or granular formations on the mucous membrane), narrowing or vice versa, gaping of the mouths of the ureters, deformation and possible displacement.

Along with the above visualization methods, the most important part of examining children suffering from various forms of megaureter is the histological examination of surgical material, which allows morphologically verifying the diagnosis and studying structural changes in the ureter tissue to further improve treatment tactics.

**Treatment. Primary reflux megaureter.** All pediatric surgeons are familiar with the standard treatment for reflux, and the treatment of primary reflux megaurether is no different. Initially, even with severe dilatation and severe reflux, medical treatment (antibiotic prophylaxis) and observation are all that is needed. Surgical intervention is considered only for persistent high reflux in older children (especially with recurrent pyelonephritis) and in children who could not receive medical treatment. Since the frequency of complications of ureteroneocystostomy is high when performed in children under the age of one year, cutaneous ureterostomy or vesicostomy can be used as a temporary measure in children requiring surgical intervention [18].

**Secondary reflux or obstructive megaureter.** Obviously, secondary reflux must be treated, eliminating the cause of increased intravesical pressure leading to reflux. For example, in children with posterior urethral valves and reflux, valve ablation and proper treatment of the bladder often lead to a rapid resolution of reflux. Neurogenic bladders with elevated detrusor leakage point pressure (> 40 cm mm.wat.) should be treated with a combination of drug therapy (i.e. anticholinergic treatment), clean intermittent catheterization, and surgery if necessary. Often, cases of prune stomach and diabetes insipidus can be controlled by observation, suggesting that appropriate drug therapy is starting [18].



Non obstructive or obstructive megaureter. In cases where a megaureter may possibly be difficult, the decision to have surgery is difficult. Even in cases of obvious obstruction, early surgical intervention is fraught with a higher complication rate. The basic principle that should be observed is that no surgery should be performed unless renal function is significantly affected and urinary tract infections are not a serious problem. Instead, suppression of antibiotics under close observation is all that is required. As a rule, surgical recovery is required at the age of 1 to 2 years, if the condition worsens [1,3,18].

In some rare cases, early intervention is required. To prevent complications associated with non-reflux therapy, re-implant surgery in children, other surgical options should be considered, such as loop ureterostomy, reflux reimplantation, and even the installation of an ureteric stent. From the point of view of the formation of algorithms that make it possible to decide which of the children will need surgical intervention, no good parameters determine the children who will decide and those that will deteriorate. In general, more than 70% of cases are resolved within 2 years of observation. Although there is no correlation with any definable factors (such as the degree of hydronephrosis) for which children will need surgical intervention and which are not, there is a correlation between the age of resolution and the degree of dilatation in infants [24].

**Surgical methods.** Surgical methods used for the final treatment of reflux and obstructive megaureters include re-implantation of the ureter of the enlarged ureter. The same parameters that are used to ensure a successful operation, like the traditional re-implantation operation, are also applicable to megaureters (i.e., the ratio of the length of the tunnel 5: 1 to the diameter of the ureter). In the case of obstructive megaureters, the distal adynamic segment must be completely amputated from the ureter, and often after removal of the obstruction, the diameter of the ureter is reduced to a size that allows standard reimplantation without narrowing. However, most reflux and obstructive megaureters require narrowing in order to provide a submucosal tunnel size suitable for a child's bladder [2,3,18].

To date, surgeons have proposed more than 200 methods of surgical correction of the ureter. The choice of the method and method of surgical intervention is determined by the nature and degree of the clinical manifestation of the disease, the presence of complications, the general condition of the patient, and also the experience of treating the corresponding patients with a medical institution [12,17].

An analysis of recent literature has shown that conservative treatment of malformation does not give the desired results, it can be used in the preoperative period, since with the most competent selection of medicines it is possible to achieve remission of pyelonephritis for several weeks and very rarely for several months. However, when ascertaining normal kidney function, it is advisable to temporarily abandon surgical treatment, since it is extremely difficult to conduct a differential diagnosis between neuromuscular dysplasia of the ureter, functional obstruction of the ureter, and disproportion of its growth in young children [7,11].

Taking into account the attending physician's technical diversity and features of various techniques, their choice should be based primarily on the anatomical and functional state of the vesicoureteral anastomosis. The right choice of surgical intervention is the key to successful treatment of a child's disease caused by damage to the vesicoureteral segment. In addition, the inclusion of the method of surgical correction of the vesicoureteral segment in the algorithm of diagnostic treatment in the treatment of children with MTCT and various forms of supraventricular obstruction allows predicting the outcome of the disease in the postoperative period [17].

The most etiopathogenetically substantiated approaches for surgical treatment of lesions of the vesicoureteral segment in children are methods aimed at increasing the length of the intramural ureter by laying a submucosal tunnel. The most popular of these proposed treatment methods was the antireflux operation Politano & Leadbetter, which was introduced in 1958 [10]. The main principle of the surgical operation was to create a submucosal tunnel for implantation of the ureter, cut off from the original location of its mouth. A high percentage of positive results of this operation, reaching 95%, determined the widespread use of this technique. E.Ya. Huseynov points out that along with the length of the submucosal tunnel, the so-called "support" function of the Lieto triangle plays a significant role in the reliability of the antireflux protection of the vesicoureteral segment.

If we consider the causes of the imperfection of one or another surgical technique for correction of the vesicoureteral segment, the author relies on the following anatomical and functional criteria: the length of the intravesical part of the ureter, the lateral ectopia of the ureteral mouth, the "support" function of the Lieto triangle, the degree of the angle of entry of the ureter into the bladder.

### **Conclusion**

Thus, an analysis of the literature made it possible to determine and reveal that issues of early diagnosis and properly balanced treatment of this disease of the urinary system in children today remain among the urgent problems of pediatric surgery and urology.

### **References.**

1. Smirnov I.E., Shamov B.K., Sharkov S.M., Kucherenko A.G., Yatsyk S.P. Biomarkers in the early diagnosis of megaureter in children. *Russian Pediatric Journal* 2011; 3; 31-36
3. Hvorostov I.N., Zorkin S.N., Smirnov I.E. Obstructive uropathy. *Urology*. 2005; 4 (1): 73-76
4. Akhmedov Yu.M., Akhmedzhanov IA, Mavlyanov F.Sh. Intravesical surgical correction of the distal ureter in children. // *West. about pr.* 2006 st 205
5. Sharkov S.M., Yatsyk S.P., Fomin D.K., Akhmedov Yu.M. Obstruction of the upper urinary tract in children. Monograph. Union of Pediatricians of Russia, Moscow 2012 st 6-9
6. Yu.M. Akhmedov, I.A. Akhmedzhanov, Sh. Kh. Mavlyanov, F.Sh. Mavlyanov, K.N. Ibragimov, J.Zh. Kurbanov. X-ray planimetric methods for the diagnosis of obstructive uropathy in children. *Saratov Journal of Medical Scientific Research*, 2007
7. Pavlov A.Yu. Obstructive uropathies and severe forms of urolithiasis in children Moscow 1997
8. Ayvazyan A.V., Voyno-Yasenetsky A.M. Malformations of the kidneys and ureters. - M.: Nauka, 1988. -- 488 p
9. Atlas of pediatric operative surgery. Author: Puri P. Publisher: MEDpress-inform, 2009
10. Combined violation of the urodynamics of the upper urinary tract in children. CM. Sharkov, Yu.M. Akhmedov - *Pediatric Surgery*, 1999
11. Shokeir, A.A. and Nijman, R.J. Primary megaureter: current trends in diagnosis and treatment. *BJU Int.* 86, (2000) 861-868.
12. Manzoni, C. Megaureter. *Rays* 27, 83-85. (2002)
13. Wilcox, D. and Mouriquand, P. Management of megaureter in children. *Eur. Urol.* 34, 73-78. (1998)
14. Report of working party to establish an international nomenclature for the large

ureter. Birth Defects Orig. Artic. Ser. 13, 3-8.(1977)

15.Belman, A.B. Megaureter. Classification, etiology, and management. Urol. Clin. North Am. 1, 497-513. (1974)

16.Koff, S.A. and Campbell, K. Nonoperative management of unilateral neonatal hydronephrosis. J. Urol. 148, 525-531. (1992)

17.Friedrich, U., Schreiber, D., Gottschalk, E., and Dietz, W [Ultrastructure of the distal ureter in congenital malformations in childhood]. Z. Kinderchir. 42, 94-102. (1987)

18.Hanna, M.K., Jeffs, R.D., Sturgess, J.M., and Barkin, M. Ureteral structure and ultrastructure. Part III. The congenitally dilated ureter (megaureter). J. Urol. 117, 24-27(1977).

19.Vlad, M., Ionescu, N., Ispas, A.T., Ungureanu, E., and Stoica, C. Morphological study of congenital megaureter. Rom. J. Morphol. Embryol. 48, 381-390. (2007)

20.Lee, B.R., Silver, R.I., Partin, A.W., Epstein, J.I., and Gearhart, J.P. A quantitative histologic analysis of collagen subtypes: the primary obstructed and refluxing megaureter of childhood. Urology 51, 820-823. (1998)

21.MacKinnon, K.J. Primary megaureter. Birth Defects Orig. Artic. Ser. 13, 15-16. (1977)

22.Mackinnon, K.J., Foote, J.W., Wiglesworth, F.W., and Blennerhassett, J.B. The pathology of the adynamic distal ureteral segment. J. Urol. 103, 134-137. (1970).

23.Dixon, J.S., Jen, P.Y., Yeung, C.K., and Gosling, J.A. The vesico-ureteric junction in three cases of primary obstructive megaureter associated with ectopic ureteric insertion. Br. J. Urol. 81, 580-584. (1998)

24.Gosling, J.A. and Dixon, J.S. Functional obstruction of the ureter and renal pelvis. A histological and electron microscopic study. Br. J. Urol. 50, 145-152. (1978).

25.Hofmann, J., Friedrich, U., Hofmann, B., and Grabner, R. Acetylcholinesterase activities in association with congenital malformation of the terminal ureter in infants and children. Z. Kinderchir. 41, 32-34. (1986)

26.Summaria, V., Minordi, L.M., Canade, A., and Speca, S. Megaureter and ureteral valves. Rays 27,89-91.(2002)

27.Khoury, A. and Bagli, D. Reflux and megaureter. In Campbell-Walsh Urology. 9th ed. Wein, A.J. et al., Eds. WB Saunders, Philadelphia. (2007)

28.Berrocal, T., Lopez-Pereira, P., Arjonilla, A., and Gutierrez, J. Anomalies of the distal ureter, bladder, and urethra in children: embryologic, radiologic, and pathologic features. Radiographics 22, 1139-1164. (2002)

29.Nadira Farmanova, Shahruz Hikmatov And Lola Pulatova Studying the mineral composition of the urological composition Journal of Biomedicine and Practice2019-2-68-76 <http://dx.doi.org/10.26739/2181-9297-2019-2-9>