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ANATOMICAL AND HISTOLOGICAL ASPECTS OF DEVELOPMENT OF URETER A FETAL CADAVERIC STUDY

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Abstract

Background

The present study determines the morphometry of the fetal ureters and correlates it with the crown rump length (CRL) and the gestational age (GA) which would be a guide for their ultrasound visualization. A histological study of the fetal ureters was also carried out to highlight the epithelial and muscular components.

Material and methods

The length of the ureter was measured from the pelvi-ureteric junction up to its intravesical part. The sections of upper and lower ends of the ureters were processed histologically and were stained. The slides were observed under the light microscope with emphasis to the epithelium and the muscle coat.

Results

The length of the right ureter ranged from 26 to 44mm while on the left side it was 27 to 49mm. The transitional epithelium characterized by the superficial umbrella shaped cells was observed by 16^{th} week. A thin coat of circularly arranged smooth muscle was seen interspersed with connective tissue at 12^{th} week was observed which was arranged into an inner longitudinal smooth muscle layer by 36th week. The epithelial and muscle components were similar in the upper and the lower ends of the ureter. An outermost longitudinal muscle layer was not observed up to 36 weeks.

Conclusion

The present study did not compare the gender differences in the ureteric length. The study has given emphasis only to the epithelial and muscular components whereas the connective tissue components such as collagen and elastic fiber content and the distribution were not studied.

Introduction

The development of the ureter begins around the fifth week of gestation. A diverticulum arises from the posteriomedial aspect of the lower part of the mesonephric ducts. It then elongates to meet the metanephric blastema, thus inducing nephrogenesis. The tip of the ureteric bud dilates to form the collecting system from the ureterovesical junction (UVJ) to the level of the collecting duct. During the ascent of kidneys at sixth to ninth weeks, the ureters elongate. At approximately the ninth week of gestation, muscularization is induced. After 19 weeks, the ureter continues to grow; however, the normal ureteral diameter in the fetal population rarely exceeds 5 mm.[1] The intravesical part of the ureter is responsible for the active and passive components for prevention of vesicoureteric reflux (VUR).[2, 3] In the era of minimally invasive surgeries, the previous knowledge of ureteral length allows a correct planning of a reconstructive surgery or ureteral reimplantation.

The lumen of ureter is lined by transitional epithelium (urothelium), which is thrown up into folds in the relaxed state.[4] Early in the development of the ureteric epithelium, the mesenchymal arrangement in the ureteric bud is only one cell layer thick and has a circular arrangement. Although the ureteric muscle should be viewed as a single muscle sheath during developmental period, there is a tendency for layering, particularly in the proximal ureter where the inner fibres tend to be longitudinal and the outer fibres circular.[5]

There's a preconception that the fetal ureters are rarely visible during antenatal ultrasound. The length of the ureters could be correlated to the crown rump length (CRL) for an accurate knowledge of the normal ureteric development. Therefore the present study determines the morphometry of the fetal ureters and correlates it with the CRL and the gestational age (GA) which would be a guide for their ultrasound visualization. A little is known about the histogenesis of the ureters as there are discrepancies in the muscular histogenesis of their upper and lower ends. Therefore a histological study of the fetal ureters was also carried out to highlight the epithelial and muscular components.

Material and methods

The present cross sectional study was carried out in the department of Anatomy, Kasturba Medical College, Manipal. Spontaneously aborted and stillborn fetuses with known GA and crown rump length (CRL) were procured from the department of Obstetrics and Gynecology, Kasturba Hospital after taking informed consent from the person concerned. Fetuses with any external malformations were excluded from the study. The ethical approval was obtained from the Institutional Ethics Committee (IEC).

The GA of fetuses ranged from 12 to 36 weeks. The study included 12 fetuses of which 8 males and 4 females. The abdomen was opened using a midline incision and the intestines were reflected to visualize the kidneys and ureters. The kidneys along with the ureters and the urinary bladder were resected.
The length of the ureter was measured from the pelvi-ureteric junction up to its intravesical part as shown in Figure 1.
The length of the ureter was correlated with the CRL using Pearson's correlation test.
Two transverse sections from each ureter were taken, one from the upper end and the other towards the urinary bladder. The sections were processed histologically and were stained using Hematoxylin and Eosin. The slides were observed under the light microscope with emphasis to the epithelium and the muscle coat. The changes were observed according to the three trimesters.

Results

The study included 12 formalin fixed fetuses of known GA and CRL. The GA ranged from 12 to 36 weeks. The CRL ranged from 19 to 31.5cm. The length of the right ureter ranged from 26 to 44mm while on the left side it was 27 to 49mm.
The length of the ureters was correlated with the GA and the CRL using Pearson's correlation test. There was a statistical significant correlation between the ureteric length and CRL ($r=0.8$, $p<0.001$) and with the GA ($r=0.9$, $p<0.001$).
As there was a significant correlation between the parameters, linear regression was applied and a regression equation was obtained for calculation of the ureteric length.
Length of right ureter in mm=0.98×GA in weeks+14.73
Length of left ureter in mm=0.75×GA in weeks+18.73

The microstructure of the ureter was studied under the light microscope in all the three trimesters.
Microstructure of the upper end:
When observed under 10X the ureter of 12 weeks GA (figure 2), it was lined by stratified epithelium with superficial flattened cells. The lamina propria was well differentiated with the presence of abundant connective tissue and blood vessels. A thin coat of circularly arranged smooth muscle was seen interspersed with connective tissue. Transitional epithelium with superficial umbrella shaped cells was distinguished by 16th week and also

appearance of an inner longitudinal smooth muscle layer was observed. By 36th week the epithelial and the muscular components were well differentiated (figure 3).

Microstructure of the lower end:

The epithelial and muscle components were similar to that of the upper end but the thickness of the muscular layer appeared thicker when compared to the upper end. An outermost longitudinal muscle layer was not observed up to 36 weeks.

Discussion

The literature review revealed a number of studies on the ureteric morphometry and histogenesis. A study by Hruby et al measured the ureteric length in adults which ranged from 14 to 37 cm. There was no statistical significant difference between men (25.05 ±3.27 cm) and women (26.73 ± 4.84 cm). [6, 7] Hugo et al studied the length of ureter in adults which was 25.36 ± 3.67 cm. No gender differences were observed.[8]

There are studies correlating the height of the individual and the ureteric length. Breauet al and Jeon et al also reported weak correlations between height and ureteral length. [9, 10] Shah et al and Pilcher et al found no correlations between height and ureteral length.[11, 12]

A study by Costa et al on anencephalic fetuses observed that the bladder nerves could be modified due to cerebral lesions with consequent brain control damage in bladder nerves. This could lead to structural alterations in anencephalic fetal bladders and ureters.[13]

Very limited literature is available on the morphometry of the normal fetal ureters. In the present study the length of the ureters correlated positively with the GA and CRL with statistical significance. As it is difficult to locate the ureters during antenatal USG it would be useful to calculate the ureteric length by knowing the GA and CRL which was obtained by a regression equation in the present study.

According to Crelin, early in the development of the ureteric epithelium, the mesenchymal arrangement in the ureteric bud is only one cell layer thick and has a circular arrangement. During the first trimester, the epithelium and mesenchyme and outer longitudinal smooth muscle, and the outer adventitia will be completed. Tanagho described that the final arrangement of muscle fibres depends on whether the growth is primarily longitudinal or transverse. [14, 15]

Although the ureteric muscle should be viewed as a single muscle sheath, there is a tendency for layering, particularly in the proximal ureter where the inner fibres tend to be longitudinal and the outer fibres circular. A purely circular arrangement of fibres is more likely to be found in the upper ureter. [5]

In the present study the authors observed a stratified epithelium lining the ureters during the first trimester. A well differentiated transitional epithelium was observed by 16th week. The circular muscle layer appeared as early as 12th week whereas an inner longitudinal muscle layer appeared by 16th week both in the upper and lower ends. The outer most longitudinal muscle layer was not observed till 36 weeks of gestation.

The present study did not compare the gender differences in the ureteric length. The morphometry of the intra-vesical part of the ureter was not included in the study. The study has given emphasis only to the epithelial and muscular components whereas the connective tissue components such as collagen and elastic fiber content and the distribution were not studied.

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Figure legends:

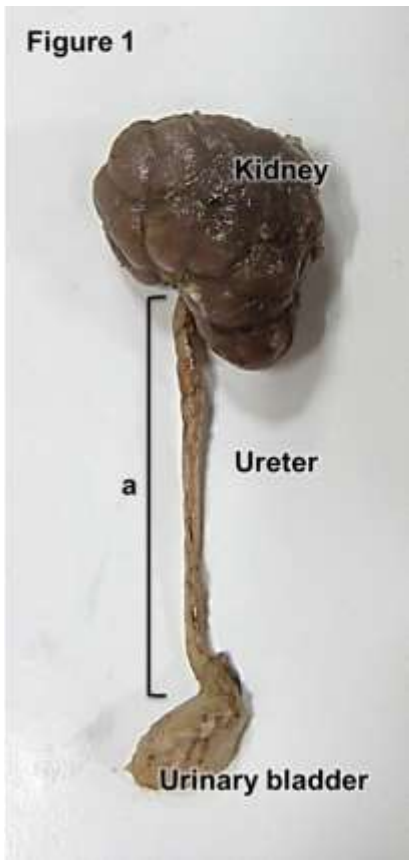

Figure 1: Specimen of the fetal kidney with the ureter and bladder. 'a' denotes the length of the ureter measured.

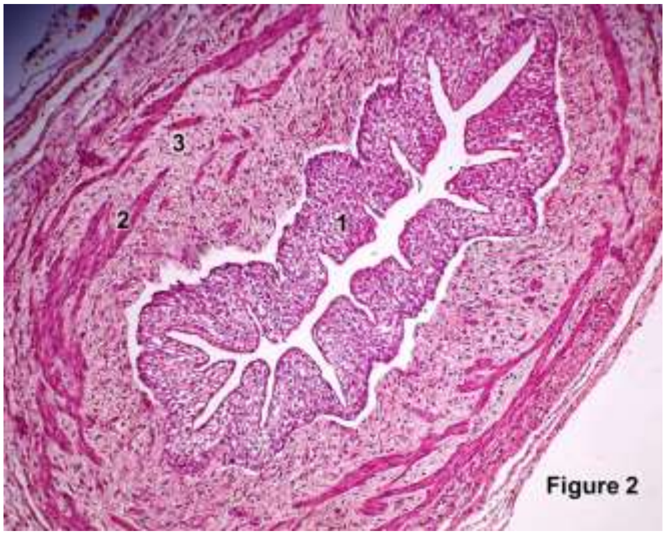

Figure 2: Section of the upper end of fetal ureter at 12 weeks of gestation. (Hematoxylin and Eosin, 10X)
1- Epithelium, 2- Circularly arranged smooth muscle, 3- Connective tissue

Figure 3: Section of the upper end of fetal ureter at 36 weeks of gestation. (Hematoxylin and Eosin, 10X)
Epithelium, 2- Inner longitudinally arranged smooth muscle, 3- Outer circularly arranged smooth muscle