

## STRUCTURE OF THE PELVIC URETER IN AN ADULT KENYAN POPULATION

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### ABSTRACT

Alterations in histomorphological features of the pelvic ureter such as muscle fiber orientation have been implicated in the etiology of vesicoureteric reflux. Consequently, anatomical sex differences in the histomorphology of the pelvic ureter may explain the female predisposition to this disease. Reports of these differences are, however, scarce. Twelve adult pelvic ureters (6 male and 6 female), harvested during autopsy were used for histomorphology. Five-millimeter thin sections were taken from juxtavesical, mid and distal intravesical segments of the ureter. These were fixed in formal saline solution and processed routinely for paraffin embedding. Seven-micrometer sections were stained with Masson's Trichrome stain to demonstrate orientation of smooth muscle cells and collagen fibers. In all sections, the ureter displayed a mucosa, muscularis and adventitia. In males, the muscularis of juxtavesical ureter displayed three layers namely an inner longitudinal, intermediate circular and an outer longitudinal. In females only two layers namely an inner longitudinal and outer circular were observed. In the mid intravesical segment, the muscularis in males displayed two layers: an inner longitudinal and outer circular layer while in females only the longitudinal layer was present. The structure of the pelvic ureter therefore displayed sex differences. In males, the muscularis in the juxtavesical and mid intravesical segments possessed additional longitudinal and circular layers respectively. These structural differences could partially explain the higher predisposition to vesicoureteric reflux in females

**Key words: Sex; histomorphology, vesicoureteric reflux, pelvic ureter**

### INTRODUCTION

The pelvic ureter is that part which extends from the pelvic brim to the urinary bladder. It consists of a juxta and intravesical segments. The latter constitutes an important mechanism for prevention of vesicoureteric reflux (VUR) (King *et al.*, 1974). This mechanism consists of passive and active components (Radmayr *et al.*, 2005). The active component comprises predominantly longitudinal muscle in the intravesical part (Thomson *et al.*, 1974), which forms anti-reflux mechanism by acting as a valve at the ostium of internal ureteric orifice (Roshani *et al.*, 1996; Shafik, 1996, 1997). In addition to the longitudinal muscle layer, a pre-vesical circular sphincter formed from the most distal circular ureteric muscle fibers has been demonstrated in an isolated study (Gil-Vernet, 1973). Thus

refluxing ureters show a reduction (Douglas, 1964) with derangement in musculature in the intra-mural segment of the pelvic ureter (Radmayr *et al.*, 2010).

Vesicoureteric reflux is five times more common in females than in males (Buckley *et al.*, 2007). Although histomorphological features of the pelvic ureter constitute important factors in protection against this condition according to Thomson *et al.*, (1994), sex differences have not been described. A histological study of the pelvic ureter would therefore provide a basis for comprehension of vesico-ureteric anti-reflux mechanisms. Further, comparison in structure of the pelvic ureter may explain the sex difference in incidence of reflux. The main aim of this study was therefore to

describe sex differences in regional histomorphology of the pelvic ureter.

## MATERIALS AND METHODS

Material for this study was obtained from 12 black adult Kenyans (ages 30 – 50 years) during autopsy at the Department of Human Anatomy, University of Nairobi, Kenya. Subjects with any visible anomalies of the ureter including trauma, females with gravid uteri, previous urinary or ureteric surgery, hydroureters and ureteroceles were excluded from the study. Ethical approval to carry out the study was granted by the Kenyatta National Hospital and University of Nairobi Ethics and Research Committee (KNH – UoN ERC) with written consent for use of autopsy specimen being obtained from relatives of the deceased.

Three 5 mm sections of the ureter were taken at the juxta-vesical, mid and distal intra-vesical portions. These were then fixed in 10% formal saline solution by immersion and routinely processed for paraffin embedding. Seven micrometer thick serial sections were cut using a Lezlar® microtome (SM2400), Germany) and stained using Masson's Trichrome to demonstrate the collagen fibers and orientation of muscle fibers (Drury *et. al*, 1976). Slides were examined using a Leica® light microscope (BME model, Germany).

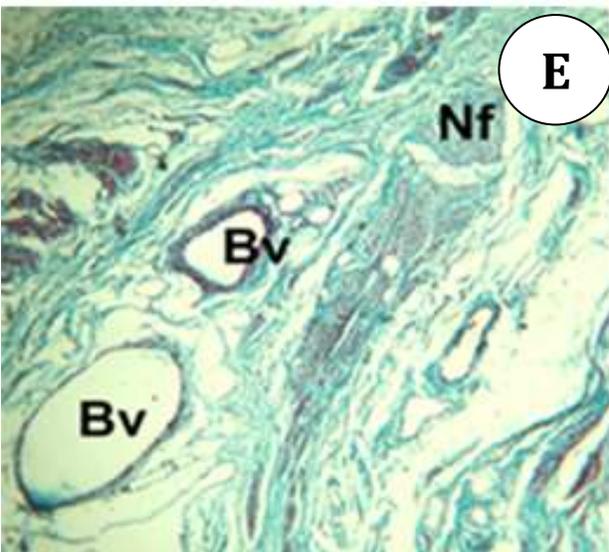
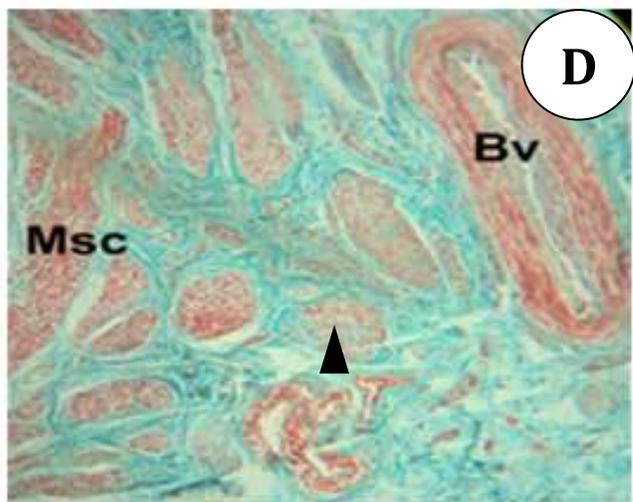
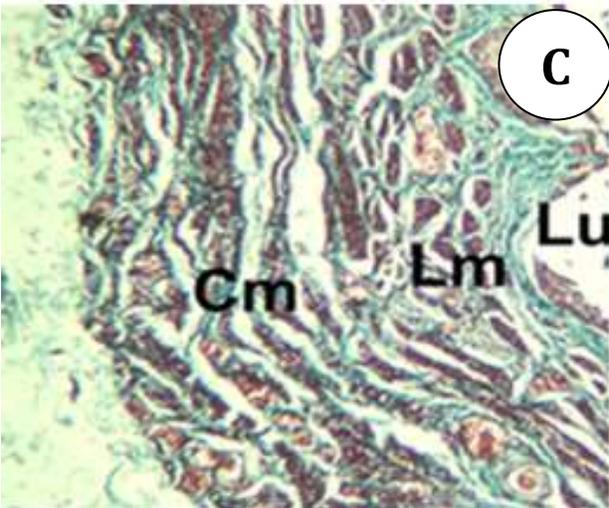
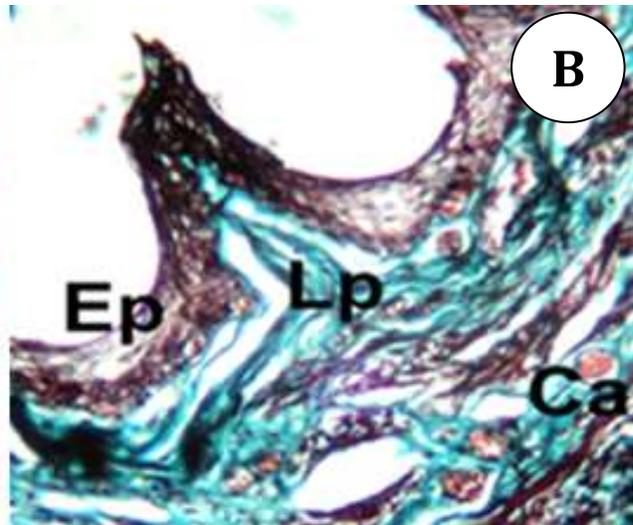
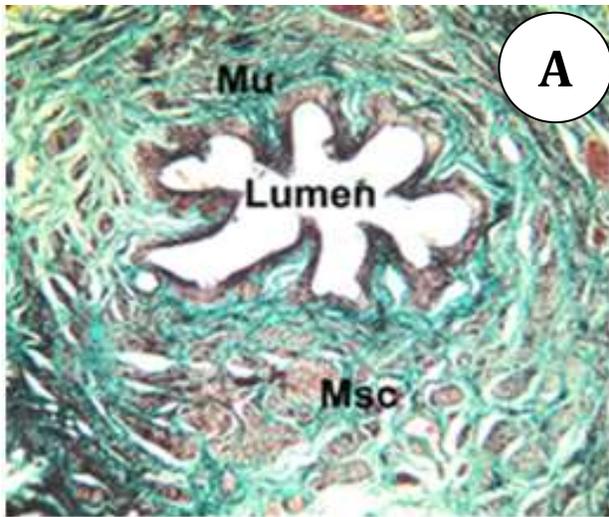
## RESULTS

### Histomorphology of the pelvic ureter

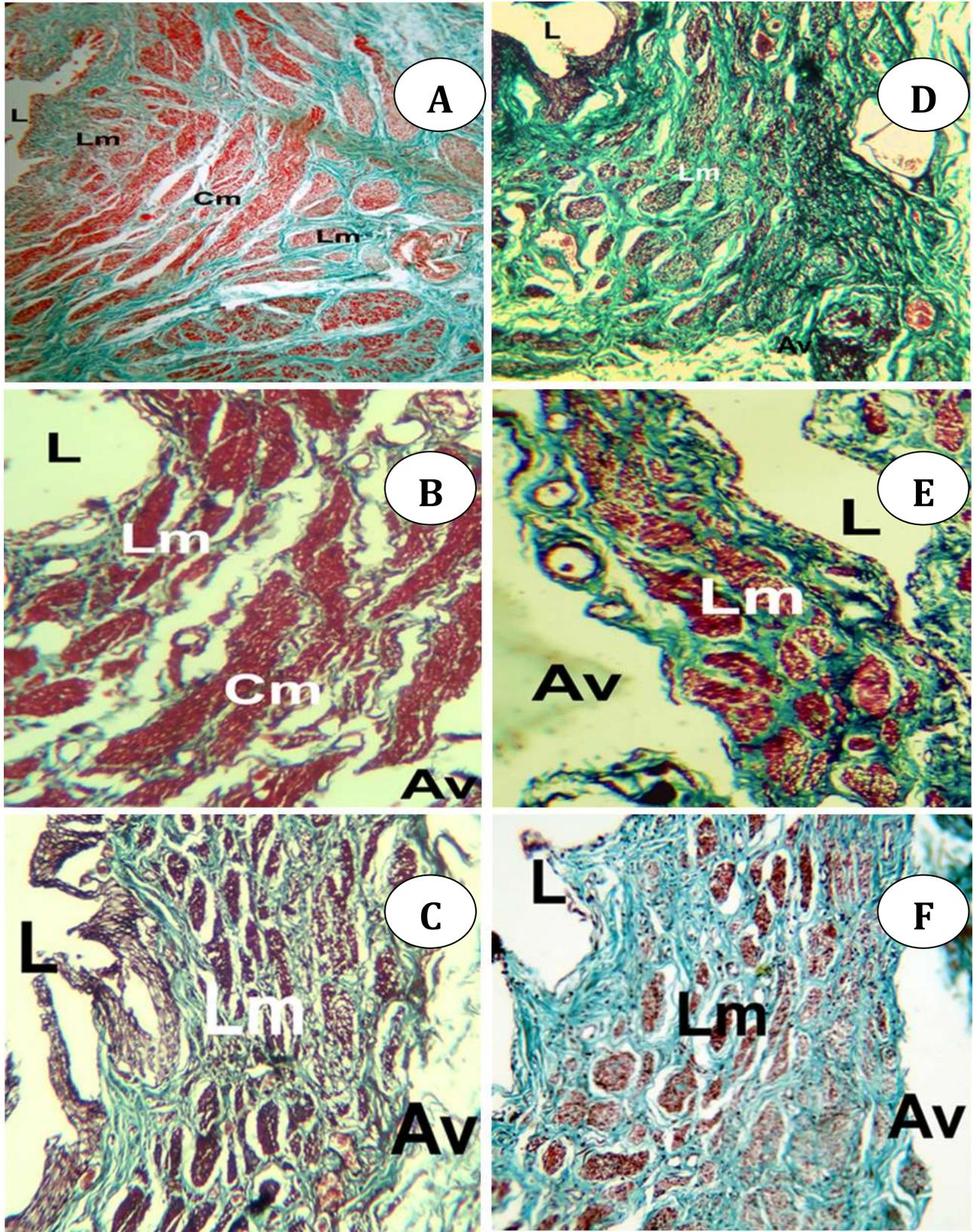
The wall of pelvic ureter comprised three layers namely mucosa, muscularis and adventitia (Fig. 1A). Its mucosa is made of transitional epithelium with predominantly cuboidal cells and an underlying lamina propria. The lamina propria consisted of dense irregular connective tissue fibers with cell aggregates (Fig. 1B). The smooth muscle cells in the muscularis layer displayed an inner longitudinal and outer circular smooth muscle (Fig. 1C). Individual muscle layers were set in bundles by connective tissue septae extending from the lamina propria. These layers were continuous circumferentially around the lumen of the ureter. Within the muscularis, blood vessels with their associated nerve fiber bundles were observed in the connective tissue (Fig. 1D). The adventitial layer consisted of loose connective tissue with adipocytes. Blood vessels were interspersed in this layer with surrounding venules and nerve fiber bundles (Fig. 1E).

### Sex differences in the pelvic ureter

The juxta-vesical ureter in the female displayed predominantly a single longitudinal muscle layer with a connective tissue septae separating it from the Waldeyer's sheath. The circular muscle layer separating the inner from the outer longitudinal muscle layers seen in males (Fig. 2A) was not distinct in females (Fig. 2B). In mid intra-vesical section, the male ureter demonstrated an additional circular muscle layer forming an incomplete ring external to the longitudinal muscle layer (Fig. 2C). The female ureter displayed predominantly single longitudinal muscle layer that was separated into bundles by connective tissue septae from the lamina propria (Fig. 2D). The muscularis of distal intra-vesical section in females consisted of a single layer of longitudinally arranged muscle layer organized in bundles (Fig. 2F). In contrast, the male ureter showed an additional circular muscle layer beyond the longitudinal layer (Fig. 2E).



**Figure 1A - E: Micrographs of transverse sections through different segments of the pelvic ureter: A:** Juxta-vesical segment of the female pelvic ureter showing its layers: Mucosa (**Mu**), muscularis (**Msc**) (Masson's Trichrome stain; x400). **B:** Juxta-vesical segment of the pelvic ureter in a female showing transitional epithelium (**Ep**) and lamina propria (**Lp**) with cellular aggregates (**Ca**) (Masson's Trichrome stain; x400). **C:** Mid intra-vesical segment of the pelvic ureter in a male showing muscle bundles: inner longitudinal (**Lm**) and outer circular (**Cm**) layers. **Lu** shows the side of the lumen (Masson's Trichrome stain; x40). **D:** Juxta-vesical segment of the pelvic ureter in a male showing a blood vessel (**Bv**) and nerve fibers (**arrowhead**) in muscularis (**Msc**) (Masson's Trichrome stain; x40). **E:** Juxta-vesical segment of the pelvic ureter in a male showing adventitial blood vessel (**Bv**), and nerve fibers (**Nf**) (Masson's Trichrome stain; x100).



**Figures 2A – F: Micrographs of transverse sections through the pelvic ureters of males and females. A:** Juxta-vesical segment of the pelvic ureter in a male showing a three-layered muscularis: From the lumen (**L**), inner longitudinal (**Lm**), intermediate circular (**Cm**) and outer longitudinal (**Lm**) (Masson's Trichrome stain; x100). **B:** Mid intra-vesical segment of the pelvic ureter in a male showing inner longitudinal (**Lm**) and outer circular (**Cm**) muscle layers. **L** shows the side of the lumen while (**Av**) is the adventitial layer (Masson's Trichrome stain; x100). **C:** Distal intra-vesical segment of the pelvic ureter in a male showing a single longitudinal (**Lm**) layer. **L** shows the side of the lumen while (**Av**) the side of the adventitial layer (Masson's Trichrome stain; x40). **D:** Juxta-vesical segment of the pelvic ureter in a female showing a single longitudinal muscle layer (**Lm**). (**L**) lumen; (**Av**) adventitia (Masson's Trichrome stain; x100). **E:** Mid intra-vesical segment of the pelvic ureter in a female showing a single longitudinal muscle layer (**Lm**). **L** shows the side of the lumen while (**Av**) the side of the adventitial layer (Masson's Trichrome stain; x100). **F:** Distal intra-vesical segment of the pelvic ureter in a female showing orientation of muscles into a single longitudinal (**Lm**) layer. **L** shows the side of the lumen while (**Av**) the side of the adventitial layer (Masson's Trichrome stain; x40)

## DISCUSSION

Histomorphology of the pelvic ureter has been implicated in etiology of vesico-ureteric reflux (Carr *et al.*, 1992). This condition has demonstrated disparity based on sex. This study therefore proceeded to describe differences in the pelvic ureter structure that probably underlie this disparity. The observations have revealed sex differences in the histomorphology of the pelvic ureter in males and females.

In males, the juxta-vesical segment had an additional outer longitudinal and a prominent intermediate circular muscle layers. This was in contrast to an inner longitudinal and an indistinct outer circular layer in females. The arrangement of muscularis in males is similar to that demonstrated for the proximal ureter (Shafik, 1997). The female juxta-vesical ureter however displayed a gradual reduction in the outer two layers of muscle with predominantly longitudinal muscle fibers. Contraction of the longitudinal muscle layer causes a reduction in length of the ureter (Roshani *et al.*, 1999) and downstream propulsion of urine bolus. This, coupled with contraction of circularly oriented smooth muscle cells will propel and inject urine through the ureter (Osman *et al.*, 2009 a,b). It is therefore plausible that the additional longitudinal muscle layer augments this function by improving delivery of bolus of urine to the next segment of the ureter.

The mid intra-vesical segment in males displayed an additional circular oriented muscle layer in comparison to the sole longitudinal layer in females. This difference is largely unreported in literature. The circularly oriented muscle bundles observed in the current study in the male intra-vesical ureter are likely to be a VUR preventing factor through peristaltic motion (Tsuchida and Kimura, 1964, 1967). These, combined with the longitudinal muscle fibers are likely to be additional features in prevention of VUR in this group. Circular oriented muscle fiber bundles in this section of the pelvic ureter have not been reported in literature. Studies cite that only the longitudinal muscle layer is present in the muscularis of the intra-vesical ureter (Douglas, 1964; Roshani *et al.*, 1996). The presence of circularly oriented muscle layers has been observed in high-pressure areas, such as the rectosigmoid junction, which demonstrates a physiologic sphincter (Shafik, 1996, 1997). The bladder is one such high-pressure system during micturition and presence of circular oriented muscles within the intra-vesical segment would suggest presence of a functional sphincter.

In both males and females, the distal intra-vesical ureter consisted of a longitudinal muscle layer. This organization of the muscular layer is in tandem with most literature reports (Peremans, 1996; Roshani *et al.*, 1996; Tanagho *et al.*, 1963, 1968).

Longitudinal muscle bundles in the intra-vesical ureter decrease length by progressive telescopic mechanism with consequent obstruction of ureteric lumen upstream of urine bolus (Roshani *et al.*, 1996). This prevents retrograde flow of urine from the bladder back into the ureter.

The pelvic ureter does indeed demonstrate sex differences in its histomorphology. Males had additional longitudinal and circular muscular layers in the juxta-vesical and mid intra-vesical segments respectively. These differences could constitute part of the underlying factors that protect against vesico-ureteric reflux in men

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