ABSTRACT

Objective: Foetal ureter is developed by ureteric bud shows many developmental changes. Normal histology of the fetal ureter at various stages of development was studied to get insight into the morphology of fetal ureter. It is necessity for correlation with increase in gestational age and pathological changes for normal functioning of urinary system in fetal life.

Method: Dissection of 87 normal human fetuses was done and histological findings of ureter were noted with respect to the age. The histology was studied by using H & E and Masson’s trichome stain. Important developmental stages were studied.

Result: chronological fetal ureteral histology is different from adult Unlike in adult ureter, oval shaped lumen shows multiple epithelial layers with circularly arranged, At 12 weeks, the smooth muscle layer was in a single layer with an abundance of interspersed collagen fibers. Vascularization increases with age in lamina propria and division of muscular layer as inner longitudinal and outer circular layer occurs. Development of transitional epithelium increased in layers by 34 weeks in the lumen. Later on, the lumen changes to star shaped by multiple mucosal folds. At 36 weeks, the thickness of the wall increased significantly with a decrease in collagen. There was no trace of longitudinal muscle fibers even upto 33 weeks.

Conclusion: Epithelial, muscular and connective tissue components displayed significant changes during intra uterine development The present study will be helpful in understanding the normal histological architecture of Foetal ureter and add to the existing knowledge regarding its development, its relation with gestational age and pathogenesis.

Key words: Transitional epithelium, lamina propria, ureteric bud, Masson’s trichome.
INTRODUCTION:
Foetal ureter is developed by ureteric bud at the fourth week of gestational age shows many developmental changes. It will develop into the definitive ureter. The bud increases in size and branches into undifferentiated mesenchyme that will form the permanent kidney. The ureteric bud will also give rise to the future major and minor calyces and the collecting tubules of the kidney (1). Normal histology of the fetal ureter at various stages of development was studied to get insight into the morphology of fetal ureter. Histologically, the ureter has three layers: (a) the mucosal epithelium which is the transitional, (b) the smooth muscle, and (c) the adventitia (2). The muscle layer of the wall of the ureter consists of inner longitudinal and outer circular with an additional layer of outer longitudinal in the lower end (3). It is necessity for correlation with increase in gestational age and pathological changes for normal functioning of urinary system in fetal life. Our aim is to find normal developmental histology of foetal ureter in chronological order.

MATERIALS AND METHODS:
Dissection of 87 normal human fetuses was done and histological findings of ureter were noted with respect to the age. Foetuses were collected and preserved in 10% formalin from obstetric department of Government medical college, Haldwani on the ethical background permitted by ethical committee of the institution. The fetuses had no visible external deformities or history of chromosomal or genetic disorders, and showed no features of maceration. The abdomen was dissected and the kidneys and ureters were identified. The whole of the ureters along with the kidneys and the urinary bladder were procured from the fetuses. Two transverse sections of the ureter were taken: one at the upper end, close to the pelvi ureteric junction and the other at the midpoint between the pelvis of the kidney and the vesico-ureteric Junction. The collected sections of each ureter were processed using paraffin embedding, and sections of 5 μm thickness were taken. The sections were subjected to haematoxylin-eosin staining to evaluate the tissue. Next, a special staining technique, namely Masson’s trichrome stain, was done so as to define the connective tissue and smooth muscle component in the ureteric wall. The microstructure of the ureter was studied under the light microscope in all foetuses having gestational age of 15 weeks to 40 weeks. Important developmental stages were studied. Histological findings of all 87 normal human fetal ureter were noted with respect to the age.

OBSERVATION AND RESULT:
The microstructure of the ureter was studied under the light microscope in all foetuses having gestational age of 18 weeks to 40 weeks-

Microstructure of the upper end:
12 week to 14 week: When the lumen of ureter was of irregular and some have enlarged oval shaped and it was lined by multilayered epithelium. The lamina propria was very thin to differentiate with the presence of connective tissue and blood vessels. A thin coat of circularly arranged smooth muscle was seen interspersed with connective tissue as shown in figure 1.
Figure 1. Transverse section of the ureter at the middle portion of ureter during 18 weeks of gestational age, Haematoxylin & Eosin stain, at 10X. L- elongated oval lumen, T- Multilayered epithelium, M- Circularly arranged smooth muscle layer, LP- thin lamina propria, C- Connective tissue.

19 week to 28 week: Collapsed lumen with arborvitae type pattern was seen mostly. Multilayered (4-5) transitional epithelium with umbrella shaped cells was distinguished. Lamina propria has been formed with rich Vacularisation and more mucosal folds had started to form. Musculature was increasing due to collapsing lumen. Muscular strands of inner longitudinal and outer circular muscle fibers were formed but not clearly differentiated in inner and outer muscular layers. While it seems that inner zone was thicker than outer zone. Blood vessel was observed and formation of connective tissue was ongoing process. Outer to muscle layer loose areolar connective tissue with blood vessel was seen in Figure 2.

Figure 2. Transverse section of the ureter at the middle portion of ureter during 26 weeks of gestational age, Haematoxylin & Eosin stain, at 10X. L- arborvitae lumen, T- transitional epithelium, LP- lamina propria with vessels, IL & OL- inner longitudinal and outer circular muscular layer, C- Connective tissue with vessels.

29 week to 34 week- An elliptical lumen of arborvitae type and somewhere irregular lumen surrounded by 5-7 layered transitional epitheliums were developed. Thick Lamina propria with more vascularised connective tissue with mucosal folds was noticed. Well differentiated Muscular organization was seen muscular strands of inner longitudinal and outer circular layer were noticed as broad band which seems to be in process of differentiation. Blood vessel and nerves embedded in loose connective tissue were noticed in outer adventitia layer, while after doing masons trichrome we can see the well developed muscle layer and abundant loose connective tissue of bluish green colour in Figure 3.
35 week to 40 week- At 38 week there were numerous longitudinal mucosal folds present in lumen which were formed due to contraction of ureteric muscle, in future that were going to take classically star shape lumen. Well developed transitional epitheliums were noticed as Outermost large cuboidal cell, intermediate polyhedral while basal were low columnar or cuboidal. Developed lamina propria was seen with dense fibro elastic connective tissue with more fibroblast cells under epithelium and within each mucosal fold there were groups of vessels and nerve while it get looser near the muscularis layer. Muscular layer was well differentiated like a broad band, which were fully developed in a multiple strands of inner smooth longitudinal with well organized outer smooth circular layer. Sometimes these muscles were embedded in between with each other and not always clearly distinct. Outermost adventitia layer was well developed with abundant loose areolar tissue with increased Vacularisation and nerves were identified Figure 4.

![Figure 3](image1)

**Figure 3. Transverse section of the ureter at the middle portion of ureter during 32 weeks of gestational age, massons trichome stain, at 10X**

![Figure 4](image2)

**Figure 4. Transverse section of the ureter at the middle portion of ureter during 38 weeks of gestational age, Haematoxylin & Eosin stain, at 10X.**

L- multiple longitudinal mucosal fold in lumen, T- 7-8 Layered transitional epithelium, LP- Thick lamina propria containing vessels in every mucosal fold,

OC-IL- Thick muscular strand of inner longitudinal and outer circular, C-Connective tissue with vessels and nerves

**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. And circular muscle layer was more prominent in upper ureter. An outer most longitudinal muscle layer was not observed up to 40 weeks.

**DISCUSSION:**

According to Crelin et al (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. During the first trimester, the
epithelium and mesenchyme and outer longitudinal smooth muscle, and the outer adventitia will be completed. Tanagho et al (5) described that the final arrangement of muscle fibers depends on whether the growth is primarily longitudinal or transverse. 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 fibers tend to be longitudinal and the outer fibers circular. Our study is supported by Ankolekar et al (6) who observed a stratified epithelium lining the ureter during the first trimester. He found well differentiated transitional epithelium by 16th week while we had observed it in 21 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 while by us circular arrangement is seen in 14 week and inner longitudinal and outer circular is differentiated by us in 22 wk clearly. The outer most longitudinal muscle layer was not observed till 36 weeks of gestation by them and we did not notice it till 40 week. Waldeyer A (7) who told the adventitia varies in thickness and is composed of areolar and fibroblastic connective tissue correlates our study as foetus is growing up the adventitia is developing and its Vacularisation is increased in term. As studied by Priya .j (8), the upper end of the ureter showed transitional epithelium 8-9 layers thick at 18 weeks. Large amounts of collagen fibers were found interspersed between a single layer of thin circular smooth muscle fiber layer. As the GA increases, the transitional epithelium increases in size The circular muscle layer also increases in thickness and the collagen fibers decreases.

CONCLUSION:

At 14 week lumen of ureter was enlarged and oval shape , in 22 weeks due to musculature getting developed it was of compressed type arborvitae shaped while in 38 weeks it seem like star shaped and multiple mucosal longitudinal folds were seen. At 14 weeks the epithelium was multilayered, stratified in 17 weeks and transitional epithelium with umbrella cells are seen in 22 weeks till 40 week. Initially at 12 week lamina propria was very thin and in 24 week it seems to be in developing phase while at 38 week it get dense with fibroblast cell and prominent Vacularisation is seen. Muscles are seen in circular manner in 14 week, by 25 week it is divided in inner longitudinal and outer circular zone. Well developed broad muscular strands were noticed at 36 week. Outer most adventitia layer is very less in initial phases while it is developed in 25 weeks and by 34 weeks it was clearly identified by abundant loose areolar tissue with increased Vacularisation and nerve fibers.

REFERENCES:


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