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### Original Article

## A study of histogenesis of human fetal kidney

Tank KC<sup>a</sup>, Saiyad SS<sup>b</sup>, Pandya AM<sup>c\*</sup>, Akbari VJ<sup>d</sup>, Dangar KP<sup>e</sup>

<sup>a,e</sup> Department of Anatomy, M. P. Shah Medical college, Jamnagar, Gujarat (INDIA)

<sup>b,c,d</sup> Department of anatomy, P. D. U. Medical college, Rajkot, Gujarat (INDIA)

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#### ABSTRACT

The normal developmental anatomy and histogenesis of urinary system helps in understanding, diagnosis and treatment of prenatal renal disorders like Wilms' tumor, multicystic renal dysplasia, hydronephroses...etc. Present study aims at studying the human kidney development by noting changes in the gross renal morphology and renal histology in fetuses of various age groups. The study was carried out at Dept. of anatomy P. D. U. Medical College Rajkot, Gujarat, India, on forty kidneys from twenty human fetuses (11 males and 9 females) of different fertilization ages ranging from 12th weeks to 36th weeks of fertilization which showed no abnormalities of the urinary tracts on macroscopic inspection. Human fetuses were procured from the Dept. of Obstetrics and Gynecology, P. D. U. Medical College Rajkot, Gujarat. After measuring foetal weight, 10 % formalin was injected in cavities and fetuses were put into 10% formalin solution. Kidneys were dissected out and after studying morphology were kept in 10% formalin, processed in paraffin, 7mm sections stained with haematoxyllin-eosin and studied under microscope. All kidneys were lobulated, bean shaped and all the dimensions of kidney increased with increase in age and weight of foetus. Histologically, the smallest glomeruli were in the most superficial cortex and the largest in the juxtamedullary zone. Size of nephrogenic zone was decreasing while size of cortex and medulla increased with increase in fetal age.

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### 1. Introduction

Prenatal development is a very crucial period for human development. It is important to know the normal developmental anatomy and histogenesis of urinary system for better understanding of various congenital renal conditions. The foetal kidney has about 12 lobes but these are fused in adults to present a smooth surface, though traces of lobulation may remain [1]. The kidney itself has an internal medulla and external cortex. The renal medulla consists of pale, striated, conical renal pyramid. Each pyramid presents a base directed to cortex and an apex which projects into the wall of renal sinus as Renal Papilla. One minor calyx receives 1 to 3 renal papillae. Each pyramid capped with adjoining cortex is known as the Lobe of Kidney. Estimates of papillae and hence of pyramids or renal lobes are variable [1].

Microscopically the kidney is composed of many tortuous closely packed uriniferous tubules bound by little connective tissue in which run blood vessels, lymphatic and nerves. Each tubule consists of two embryologically distinct parts, secreting part i.e. nephron which elaborates urine and collecting part i.e. collecting tubules. Kidneys develop in intermediate mesoderm of human embryos in cranio-caudal direction. These are pronephric kidney, mesonephric kidney and metanephric kidney. The development of the kidneys illustrates the famous dictum of Haeckel (1874) [1] that "ontogeny recapitulates phylogeny". This means that the development of the three kidney types follows an evolutionary pattern. Metanephros is the primordia of permanent kidneys. It appears in lumbosacral segments. They develop early in 5th week and start to function around 9th week. It develops from 2 sources metanephric diverticulum (Ureteric bud) – forms collecting part and metanephric mass of intermediate mesoderm (metanephrogenic blastema) forms secretory part. Kupffer, found that from the dorsal wall of the Wolffian or mesonephric ducts near their posterior termination, there formed an evagination which he

\* Corresponding Author : Dr A.M. Pandya

Asst Prof., Anatomy  
P.D.U. medical College  
Rajkot, Gujarat, 360001, INDIA  
Tele: 9426239635  
E-mail: [ashishmpandya@gmail.com](mailto:ashishmpandya@gmail.com)

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designated as “Nierenkanal” known as ureteric bud [2]. Ureteric bud is a primordial of ureter, renal pelvis, calices and collecting tubules. Its distal end dilates and invades the caudal part of nephrogenic cord dorsal to mesonephric ridge. Ureteric bud repeatedly divides until about 13 or more generations of tubules are formed. ureteric bud is capped with a metanephric blastema on further sub-division some parts of the blastema separate from the main mass and form clusters of cells on each side of the tubule forms pear shaped hollow renal vesicles. First vesicle is formed at the end of 7th week in relation to 6th division of ureteric bud [3]. Cells at the proximal pole of the vesicles organize to form C-shaped or comma shaped body followed by cellular reorganization of tubular cells at distal end to form an 'S' shaped body or S-body. In the cleft of the S-body at the distal pole, formation of extra cellular matrix and penetration by capillaries targets at formation of future mesangial region. The proximal limb of the S-body organizes to form distal convoluted tubule while the intermediate limb enlarges to form loop of Henle and the proximal convoluted tubule resulting in entire development of a nephron. Many such nephrons are present in the fetal kidney due to multiple branching of the ampullary bud and induction of various mesenchymatous condensates to form nephron arcades. This process of renal development begins at deeper regions and reaches the peripheral part of the cortex with the advancement of ampulla in that region and terminates during the last month of gestation with subsequent

## 2.Material and Methods

After approval from the institutional ethical committee, 20 human fetuses were procured from the Dept. of Obstetrics and Gynaecology, P. D. U. Medical College Rajkot, Gujarat, for present study with due consent from parents. Fetuses were obtained within 1 – 2 hours of abortions to avoid post-mortem changes. Weight, crown rump length (CRL), crown heel length (CHL), foot length, bi-parietal diameter were measured to determine age of foetus and then 10 % formalin was injected in cavities and fetuses were kept in 10% formalin solution. Kidneys were dissected out and observed for location and appearance. Kidneys were kept in 10% formalin for 24 hours and then processed for dehydration, clearing, embedding and paraffin blocks were prepared. 7mm sections were taken with rotary microtome and stained with haematoxylline and eosin and observed under microscope.

Measurements from microscopic slides: Size of glomeruli was measured according to method suggested by Bridgette J et al [6]. The renal cortex was divided into three evenly spaced zones: outer (superficial glomeruli), mid and inner (juxtamedullary glomeruli) cortex. Outer cortical glomeruli were within 3–4 glomerular diameters of the capsule, while juxtamedullary glomeruli were within 3–4 glomerular diameters of the corticomedullary junction. Individual glomerulus diameter was measured in microns with the

## 3.Results

### 3.1.Morphological observations

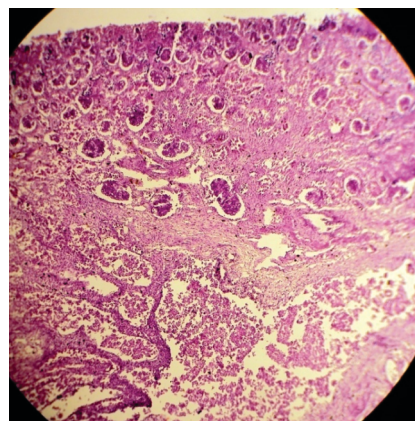
Site- In all samples kidneys were found in lumbar region bilaterally. Appearance- All kidneys were lobulated in appearance.

### 3.2.Microscopic structure of kidney

#### 12 weeks:

As shown in Photograph 1, the lobes were separated only in the superficial part of the cortex. In the deeper part of cortex they were fused with each other. The kidney was covered by a thin capsule made up of fibrous tissue. Beneath the capsule the cortico medullary differentiation was not well marked.

**Photograph 1: Showing microscopy of 12 weeks of fertilization fetal kidney.**



**Cortex:** In the superficial part of the cortex, just beneath the capsule, there was a zone of undifferentiated mesenchymal tissue having closely packed cells. This was the nephrogenic zone containing nephrogenic cells. These cells have faint eosinophilic cytoplasm and dark staining oval nuclei. In the cortex the immature developing glomeruli were more in number.

**Medulla:** The medulla contains undifferentiated mesenchymal tissue containing spindle shaped cells with pale cytoplasm and oval nuclei. At places in the medulla, the cells were arranged in groups indicating the formation of collecting tubules. The primitive blood vessels lined by simple squamous epithelium containing RBCs were seen, scattered in the medulla. The hilar region showed large blood vessels containing RBC with large amount of mesenchymal tissue and the developing renal pelvis was observed.

#### 14 weeks:

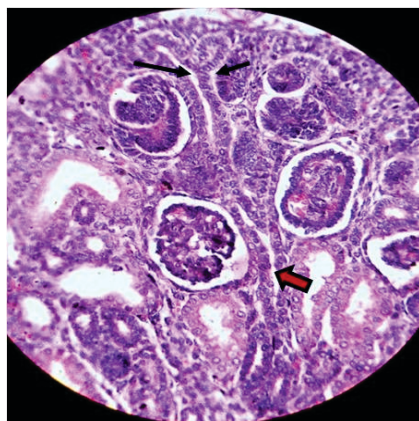
On panoramic view, the kidney showed lobulation. The lobes were separated only in the superficial part of the cortex. In the deeper part of cortex they were fused with each other. The kidney

was covered by a thin capsule made up of fibrous tissue. Beneath the capsule the cortico medullary differentiation was not well marked.

**Cortex:** In the superficial part of the cortex, just beneath the capsule, there was a zone of undifferentiated mesenchymal tissue having closely packed cells this was the nephrogenic zone containing nephrogenic cells. These cells have faint eosinophilic cytoplasm and dark staining oval nuclei.

Beneath the nephrogenic zone, the growing ureteric bud in the form of ampulla is seen. The cells of the ureteric bud were cuboidal with centrally placed nuclei. This bud was surrounded by group of cells called the nephrogenic cells which forms a cap over the ampulla. At places it had divided dichotomously into two (Photograph 2) to give next generation of tubule which was parallel to the surface of the kidney. Some cells form groups which were seen at an angle between the growing ampulla and old tubule. Deep to the nephrogenic zone, but in the superficial part of the cortex, the various stages of developing glomeruli were seen in different stages of development.

**Photograph 2: showing renal cortex of 14 weeks of fertilization fetal kidney. [Ureteric bud (red arrow) bifurcating in two (Black arrows) branches having dilated ampulla.] H&E; 45X**



In the superficial part of the cortex the ureteric buds were dividing. At the angle between the division and the old tubule, hollow structure lined by single layer of cells having central cavity were seen. These were nephrogenic vesicles. The cells had oval nucleus, arranged perpendicular to the lumen. These nephrogenic vesicles were the most primitive form of glomerulus.

At places there were 'S' shaped hollow structure, with the cavity lined by single layer of cells. It had three portions; upper which was closer to the capsule, lower towards the medulla and in between these two the middle curve. The inner wall of the lower portion having convex margin were lined by low cuboidal cells while the outer wall having concave margin were lined by tall columnar cells

In some developing glomeruli, the lower portion of the 'S' tubule had become crescentic (Photograph 2). The cells of the lower convex margin were flattened to low cuboidal with round euchromatic nucleus. Within the concavity of the crescent the mesenchymal cells were loosely arranged, and very few capillary spaces lined by endothelial cells were seen. In few glomeruli the developing capillaries had been invaginated in the crescent. The convex margin was lined by flat cells while the concave margin was lined by tall columnar cells. At some places in the glomeruli the capillaries in the Bowman's capsule showed lobulations. The parietal layer was flat while the visceral layer was of simple columnar cells with dark staining oval nuclei.

The glomeruli present in the deeper aspect of the cortex shows well marked lobulation. The visceral epithelium covering the glomerulus was formed by closely packed columnar to cuboidal cells with dark staining nuclei but it was discontinuous at places. The parietal layer was lined by squamous cells. In the deeper part of the cortex the glomeruli were present in mature form. In the Bowman's capsule the network of glomerular capillaries were seen. The visceral layer of the Bowman's capsule showed only few cells scattered over the surface of the glomerular tuft. The parietal layer was of squamous cells. These were the mature glomeruli.

Over all, in the cortex the immature developing glomeruli were more in number as compared to mature forms. The immature glomeruli were seen in the superficial part of cortex while the mature glomeruli with lobulated capillaries were present in deeper cortex. In between the developing glomeruli within the connective tissue, the developing tubules were seen. They were lined by cuboidal cells with pale eosinophilic cytoplasm and vesicular nuclei. These were developing tubules which cannot be differentiated into proximal or distal convoluted tubules.

**Medulla:** The medulla contained undifferentiated mesenchymal tissue containing spindle shaped cells with pale cytoplasm and oval nuclei. At places in the medulla, the cells were arranged in groups indicating the formation of collecting tubules. Only in some developing tubules the lumen was seen. The primitive blood vessels lined by simple squamous epithelium containing RBC were seen, scattered in the medulla.

The hilar region showed large blood vessels containing RBC with large amount of mesenchymal tissue and the developing renal pelvis was observed.

#### 16 weeks:

Nephrogenic zone containing undifferentiated nephrogenic cells were seen but it was reduced in thickness as compared to the previous stage.

**Medulla:** In medulla, irregular tubules of various dimensions, in between the connective tissue were seen. Some were lined by columnar cells with clear cytoplasm and vesicular nuclei. These were probably the collecting tubules. Few tubules of smaller dimension lined by simple cuboidal cells with eosinophilic cytoplasm and round nuclei were seen. These might be thick

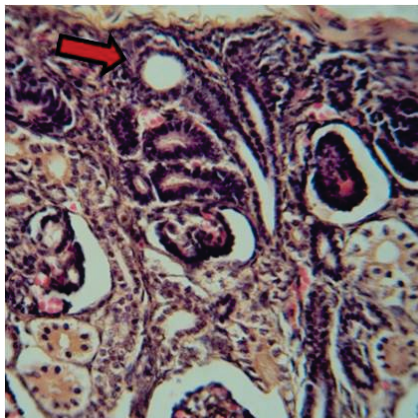
segments of the loop of Henle. In between the tubules the blood vessels lined by endothelium containing the RBCs were seen.

At the hilum of kidney the renal pelvis lined by transitional epithelium was seen.

#### 17 weeks:

**Cortex:** Beneath the capsule the nephrogenic zone was reduced in thickness. The cortex and the medulla can be better differentiated than the previous stage. At some places the proximal and distal convoluted tubules can be identified (Photograph 3). Few tubules showed large pyramidal cells with intense eosinophilic cytoplasm with brush border and round euchromatic nuclei. These were proximal convoluted tubules. Few tubules were lined by simple cuboidal cells with pale eosinophilic cytoplasm and round euchromatic nuclei. These were the distal convoluted tubule. They had wider lumen as compared to the proximal tubule. These tubules were better differentiated in the deeper part of the cortex. Rest of the tubules in the cortex were in undifferentiated form.

**Photograph 3: 17 weeks of fertilization fetal kidney cortex H&E; 45X [Arrow: Renal vesicle]**



**Medulla:** In the medulla, the numbers of tubules were increased and the connective tissue was decreased. The collecting tubules were of larger diameter and lined by columnar cells. The tubules having cuboidal epithelium were the thick segments of loop of Henle and those lined by squamous epithelium and having small lumen were the thin segment of loop of Henle. The vascularity of the kidney was increased compared to the previous stage as indicated by more RBCs, both in cortex and in the medulla. The RBCs were present within the capillaries.

#### 22 weeks:

**Cortex:** The subcapsular nephrogenic zone was seen but it was reduced in thickness as compared to the 18 weeks. The cortex appeared more mature. The numbers of glomeruli were increased. The number of mature glomeruli were increased which were

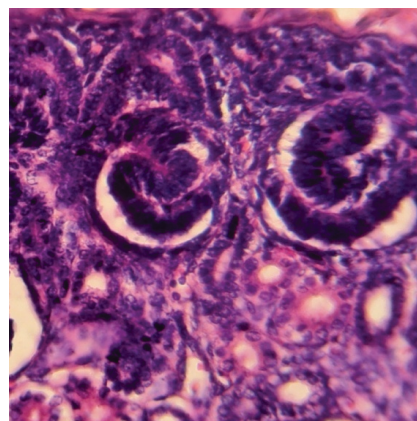
present in the deeper part of the cortex and less number of developing glomeruli were seen in superficial cortex. At higher magnification the PCT and DCT can be easily identified (Photograph 4). They showed their different characteristic staining pattern.

**Medulla:** The medulla was increased in thickness. It shows more number of collecting tubules. The amount of connective tissue was decreased.

The vascularity of both cortex and medulla was increased.

The renal pelvis can be identified by the transitional epithelium.

**Photograph 4 : Show 22 weeks of fertilization fetal kidney cortex H&E; 45X.**



#### 24 weeks:

Cortico medullary differentiation had become more distinct.

**Cortex:** More number of PCT and DCT were identified. In between this few undifferentiated tubules and less amount of connective tissue were seen.

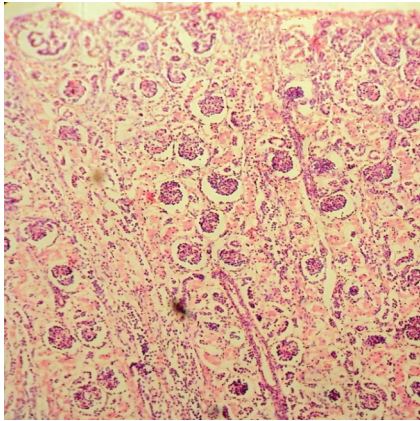
**Medulla:** In medulla more number of collecting tubules and thick and thin segments of loop of Henle were seen. The connective tissue had reduced in amount. Collecting tubules in the superficial medulla were lined by simple cuboidal epithelium. In the deeper part; the lining epithelium was columnar with round nuclei placed at the basal region, these were duct of Bellini.

#### 30 weeks:

Well differentiated cortex and medulla was seen. The thickness of cortex and medulla were increased.

**Medulla:** Medulla of kidney appeared more mature. The number of collecting tubules and thick and thin segment of loop of Henle were increased. In the deeper part of medulla close to renal pelvis, the duct of Bellini, lined by columnar epithelium were seen. (Photograph 5)

**Photograph 5: Show 30 weeks of fertilization fetal kidney cortex H&E; 10X.**

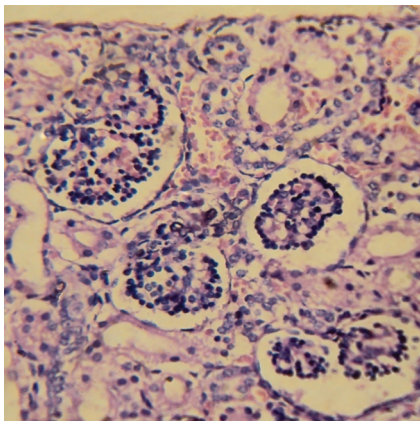


**36 weeks:**

**Cortex:** The nephrogenic zone beneath the capsule was not seen. The cortex contains mature glomeruli with lobulated capillaries present just beneath the capsule (Photograph 6). The vascularity of the cortex was also increased.

**Medulla:** The medulla shows well differentiated collecting tubules and thick and thin segment of loop of Henle. Close to the renal pelvis, the ducts of Bellini with columnar epithelium were identified.

**Photograph 6: Show 36 weeks of fertilization fetal kidney cortex H&E; 45X.**



Average Glomerular size in inner, middle and outer zone of

**Table 1: Showing fertilization age in weeks and average glomerular size in inner, middle and outer zone.**

Weeks of fertilization	Average outer glomerular size	Average middle glomerular size	Average inner glomerular size
12	40.57	46.05	50.60
13	35.75	38.77	41.93
14	46.76	51.99	59.78
15	43.32	53.44	65.26
16	44.32	52.40	63.55
17	45.81	55.64	64.68
18	44.95	52.09	62.22
22	44.82	53.45	62.56
24	41.94	44.68	51.17
28	42.53	52.75	64.49
30	45.51	53.98	63.90
32	46.88	55.70	63.93
36	49.25	56.35	62.91

**4. Discussion**

The human foetal kidneys showed lobulation which was well marked in early weeks of fertilization, as weeks of fertilization increased, lobulations were less marked. The lobes were separated only in the superficial part of the cortex. In the deeper part of cortex they were fused with each other. The kidney was covered by a thin capsule made up of fibrous tissue. Beneath the capsule the cortico medullary differentiation was not well marked in lower weeks of fertilization, as weeks of fertilization increased cortex and medulla were very well differentiated. The thickness of cortex and medulla were increased with increase in weeks of fertilization. Histological findings of present study were comparable with the study of Daković-Bjelaković M et al [7].

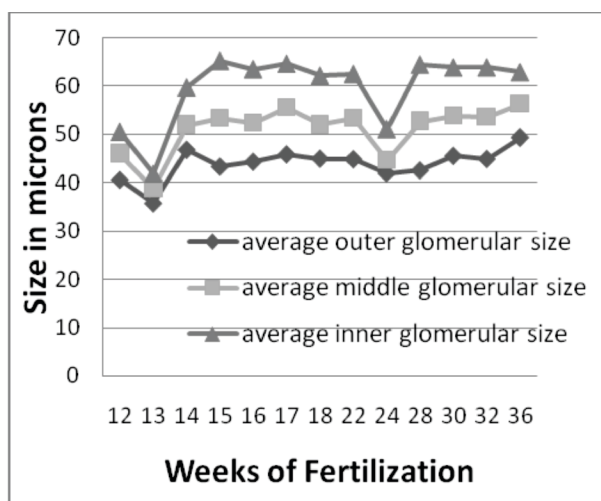
**Cortex:** In the superficial part of the cortex, nephrogenic zone was very large at lower weeks of fertilization but as weeks of fertilization increased size of nephrogenic zone decreased, it was absent at 36 weeks of fertilization. Nephrogenic cells had faint eosinophilic cytoplasm and dark staining oval nuclei indicating rapid cell division.

Beneath the nephrogenic zone, the growing ureteric bud in the form of ampulla was seen. The cells of the ureteric bud were cuboidal with centrally placed nuclei. This bud was surrounded by group of cells called the nephrogenic cells which forms a cap over the ampulla. At places it had divided dichotomously into two, to give next generation of tubules which were parallel to the surface of the kidney. Some cells form groups at an angle between the growing ampulla and old tubule.

Deep to the nephrogenic zone, but in the superficial part of the cortex, the various stages of developing glomeruli were seen in different stages of development. In early weeks of fertilization, the numbers of matured glomeruli were less and immature glomeruli were many which were present just beneath the capsule. As weeks of fertilization increased number of mature glomeruli increased which were present in deeper parts of the cortex (Chart 1). Scattered glomeruli were found near the arcuate vessels as in the study of Emery J.L., Macdonald M.S. [8], which states that the scattered glomeruli were found in two zones; one near the arcuate vessels and the other near the capsule. It is suggested that the scattered glomeruli in the arcuate vessels represent involution forms of large glomeruli which formed very early in this region in intra-uterine life, and possibly represent a transitory renal structure; peripherally situated scattered glomeruli may be related to disease processes occurring during the later development of the fetus or in the period immediately following birth [8].

In earlier weeks of fertilization in between the developing glomeruli within the connective tissue, the developing tubules were seen; as weeks of fertilization increased they differentiated into proximal or distal convoluted tubules.

**Chart-1 :Showing average glomerular size of outer, middle, inner zone of cortex at different weeks of fertilization with age of Fetus in weeks.**

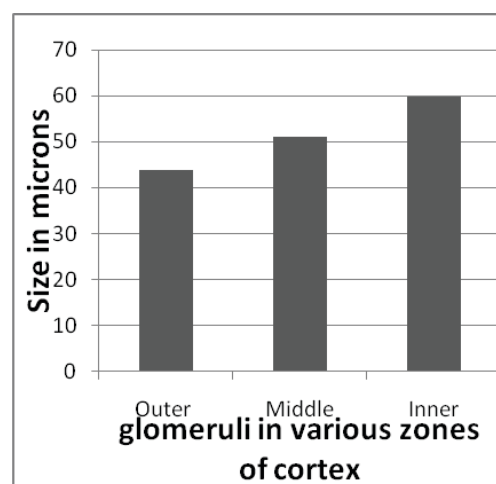


**Medulla:** The medulla contains undifferentiated mesenchymal tissue containing spindle shaped cells with pale cytoplasm and oval nuclei. Undifferentiated mesenchymal tissue decreased with increase in fertilization age. At places in the medulla, the cells were arranged in groups indicating the formation of tubules. At 17 weeks of fertilization tubules were first time clearly demarcated as proximal and distal convoluted tubules. As the age of fetus increased the numbers of mature tubules were increased and the connective tissue was decreased. With increase in age of fertilization vascularity of both cortex and medulla was increased.

At the hilum of kidney the renal pelvis lined by transitional epithelium was seen.

In present study, glomeruli of smallest size were present in the outer zone of cortex and size increases as we go to middle zone and then to inner zone (Chart 2). The size of the glomeruli in particular zone at various age groups does not change much. These finding correlate with the findings of Shimada K, et al, [9] who reported that the glomeruli were arranged in the uniform fashion on the medullary ray with the smallest in the most superficial cortex and the largest in the Juxtamedullary zone. The superficial glomeruli remained at the surprisingly same size up to birth. Juxtamedullary glomeruli showed no significant differences before birth, either.

**Chart 2: Showing average glomerular size of outer, middle, inner zone of cortex.**



The glomerular size in all three zones in Daković-Bjelaković M [10], study was bigger than present study and also glomerular size in particular zone increases with increase in age which does not match to our study. Smaller size in present study may be because we have done tissue embedding in paraffin wax. In paraffin embedded material shrinkage can be around 25% and compression around 10% relative to the fresh material [11].

## 5. Conclusion

Present study showed that fetal kidneys ascend to its adult position before 12 weeks of fertilization; they were lobulated, bean shaped and all the dimensions of size increased with increase in age.

Histologically the glomeruli were arranged in such a way that the smallest in the most superficial cortex and the largest in the juxtamedullary zone. The mean glomerular size in outer, middle and inner zone of cortex were 43.8 microns, 51.5 microns and 59.7 microns respectively and it remained nearly same in a particular zone of cortex at different weeks of fertilization from 12 to 36 weeks of fertilization. Nephrogenic zone was observed up to 32 weeks of fertilization. Size of nephrogenic zone was decreasing while size of cortex and medulla increased with increase in fetal age. Proximal convoluted tubule and distal convoluted tubule were clearly first time demarcated at 17 weeks of fertilization.

## 6. References

- [1] Dyson M. Urinary System In: Gray's anatomy. Williams P. L., Bannister L.H., Berry M.M. Collins P. et al.(eds). 38th ed. Churchill Livingstone, Newyork, Edinburgh, London, 1995, pp 1815-1828
- [2] Carl Hubber. Development and shape of uriniferous tubules of certain higher mammals, American journal of Anatomy. 1905; 4(suppl);1. (KUPFFER C.-Untersuchungen uber die Entwicklung des Ham- und Geschlechtssystems. Arch. mikr. Anat., Bd. I, 1865)
- [3] Sabita mishra, Anant Dinesh, J.M. Kaul, Morphological and morphometrical study of human renal development during mid-gestational period, JASl. 2006; 55(2): 5-10
- [4] Almeida JR, Mandarim-de-Lacerda CA. Quantitative study of comma shaped body, S-shaped body and vascularized glomerulus in the second and third human gestational trimesters. Early Human Development. 2002; 69: 1-13.
- [5] Osathanondh V, Potter EL. Development of Human Kidney as Shown by Microdissection. I. Preparation of tissue with Reasons for possible misinterpretations of observations. Arch Pathol. 1963; 76: 271-276
- [6] Bridgette J. Mc Namara et. al. Association between age, body size and nephron number with individual glomerular volumes in urban west African males. Nephrol dial Transplant (2009); 24: 1500-1506
- [7] Daković-Bjelaković M, Vlajković S, Cukuranović R, Antić S, Bjelaković G, Mitić D. Quantitative analysis of the nephron during human fetal kidney development. Vojnosanit Pregl. 2005; 62(4): 281-286.
- [8] Emery J. L., Macdonald M. S., Involuting and scattered glomeruli in the kidneys of infants. American journal of pathology. 1960; 36: 713-722
- [9] Shimada K, Hosokawa S, Tohda A. Nippon Hinyokika Gakkai Zasshi. 1993; 84(12): 2091-2096.
- [10] Daković-Bjelaković M, Vlajković S, Cukuranović R, Antić S, Bjelaković G, Mitić D. Changes of the glomerular size during the human fetal kidney development. Srpski Arhiv za Celokupno Lek. 2006; 134(1-2): 33-39.
- [11] Carlos A. Mandarim-DE-Lacerda. Stereological tools in biomedical research. Anais da Academia Brasileira de Ciências. 2003; 75(4): 469-486.