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Original Article

STUDY OF HUMAN FETAL KIDNEY

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ABSTRACT

Background: The knowledge of the basic human morphology and developmental anatomy is very imperative for diagnostic and therapeutic procedures. The question of study of human renal development arose for prenatal diagnosis of congenital malformations. There are few reports regarding the morphological development of human kidney, So, our study aims at contributing to the knowledge of morphogenesis and histogenesis of human kidney. At various gestations.
Materials and method: 30 human fetal kidneys between 10 to 34 weeks of gestation were dissected and processed in paraffin, 7mm thick sections were stained with Haematoxylin-Eosin and Masson's Trichrome stains. They were divided into 5 groups according to CRL and light microscopy examination done**.**
Results: Morphogenesis of human kidney starts at 5th week of gestation and extends upto last month of last trimester of pregnancy, renal pelvis was very small and undifferentiated at 10 weeks and fully differentiated at 18 weeks. Zone of transition between cortex and medulla appeared at the starting of 14 weeks, presence of lobulation in kidneys was observed as early as 10 weeks, lobules start fusing with each other at 15 weeks of gestation. An arcade system along with well-defined pyramids was observed at 16-18 weeks.
Conclusion: The present work made an attempt to do detailed light microscopy of human kidney at various stages of gestation, the data on which is scanty in Indian population.
KEY WORDS: Kidney, lobules, arcade, pyramid, pelvis.

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INTRODUCTION

The emphasis on genetic counseling and possibility of early prenatal diagnosis has stimulated interest in fetal kidney anatomy [1]. Definitive human kidney is derived from the mesonephric duct (ureteric bud) and metanephric blastema. Local mesenchyme migrates into metanephric blastema to form glomeruli and vasa recta. In brief, the ureteric bud developing from the mesonephric duct dilates and forms ampulla. The mesenchymatous tissue epithelises and forms vesicles which fuse with the ampulla to form a nephron. Metanephric development begins around 5th week of IUL and terminates in the last month of 3rd trimester of pregnancy with subsequent interstitial growth. Many such nephrons are present in 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 [2].

The result of these sequence of developmental events is that the external surface of fetal kidney shows grooves which correspond to the lobulat-

ion of the organ. Normally, these grooves may disappear as a result of fusion of lobules but occasionally may persist into adult life. By 90 days (90mm C.R.Length) the metanephros shows differentiation into a cortex and a medulla [3].

Since there are very few reports in regard to developing human kidney, the following study was conducted with an aim to study of histological changes during development of kidney and study of time of differentiation of cortex and medulla.

MATERIALS AND METHODS

The study was conducted in the Department of Anatomy, Govt. Medical College, Jammu, India. Still born and aborted fetuses were collected from the operation theatre, labour room and Obstetric wards of Department of Obstetrics and Gynaecology, Government Medical College Jammu, Government Hospital Gandhi Nagar, Government Hospital Sarwal and various nursing homes operating in and around Jammu city.

TABLE 1: Gestational age based on Crown Rump Length.

Groups	Crown-Rump Length (In mm)	Age (In weeks)	No of fetuses
1	53 to 58	10 to 11	2
2	75 to100	12 to 15	5
3	111 to 140	16 to 18	12
4	145 to177	19 to 22	6
5	180 to300	23 to 34	5

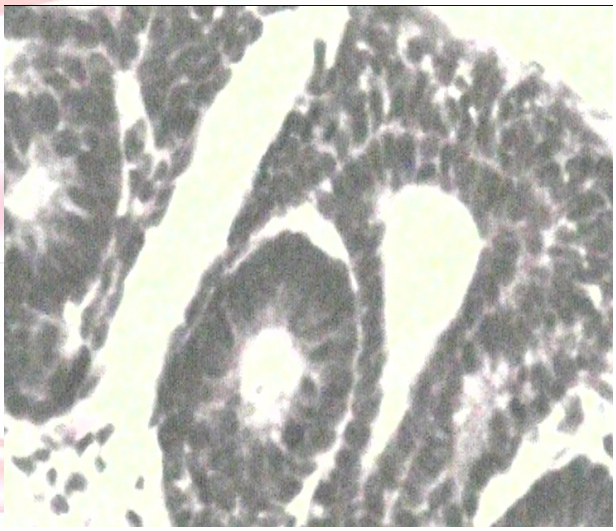
Specimens having any type of congenital malformations were not taken up for the study. A total of 30 fetuses were selected and grouped into 5 groups according to their CR length. Youngest fetus with CR Length 53 mm and oldest with CR Length 300mm as shown in table 1.

After naked eye examination of fetuses,kidneys were dissected out and their crown rump length was measured using Vernier Calliber. They were immersed and fixed immediately in 10% formalin solution. All were in excellent condition of preservation and none of them had any congenital malformation. Entire kidneys were embedded en bloc in paraffin using standard protocol.Tissue blocks were serially sectioned to generate 5-8 µ thick sections using Rotary microtome. The sections after mounting were stained with H&E and Masson's Trichrome stains.

OBSERVATIONS

GROUP 1 – 10 TO 11 WEEKS: Kidney of 10 weeks old fetus was very small and lobulated. The distal ends of Primary collecting tubules dilated to form the ampulla. Ampulla was lined by a single layer of cylindrical cells and was surrounded by double layer of metanephrogenic tissue. Outer layer of this metanephrogenic tissue was seen blending with the surrounding mesenchymatous tissue.Beneath ampulla a renal vesicle lined by single layer of columnar cells was seen (Fig 1)

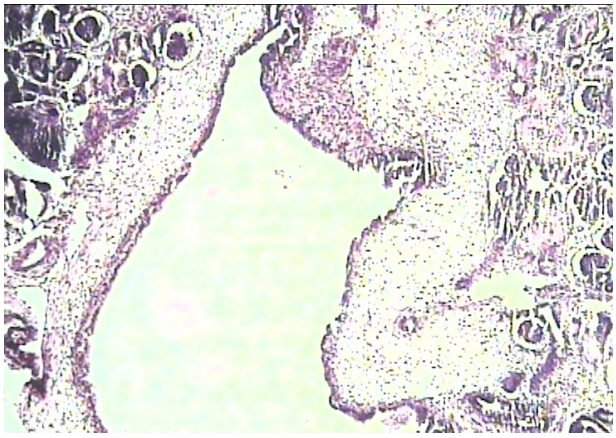
Fig. 1: Ampulla and Renal vesicle in a 10wks old fetus in Masson's trichrome X 40



No differentiation is seen between cortex and medulla at this stage.

Hilar region shows a developing pelvis lined by single layer of epithelial cells with round nuclei. Immediately surrounding the pelvis, there is a layer of dense mesenchymatous tissue.

Fig. 2: Showing pelvis and major Calyces at 11 wks of gestation in H&E X 4.

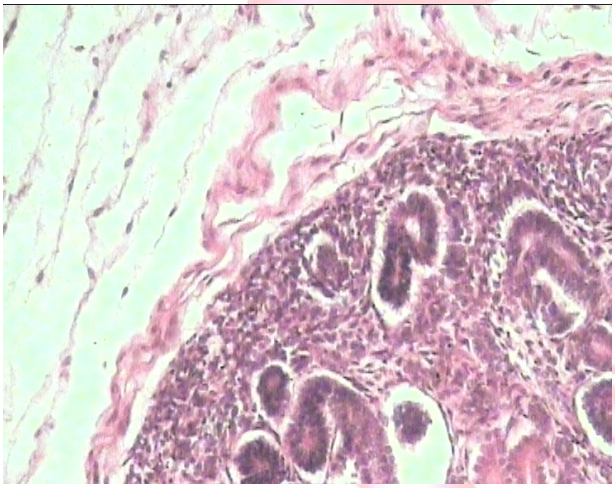


At 11wks, a larger dilated pelvis dividing into 3 to 4 Major calyces are seen. Major calyces were seen dividing into slender and tubular Minor calyces (Fig2).

GROUP 2 – 12 TO 15 WEEKS: At 12 to 13 weeks, kidney was larger and showed lobulation. These lobules were separated from each other by mesenchymatous tissue.Periphery of the kidney showed many branching ampullae.

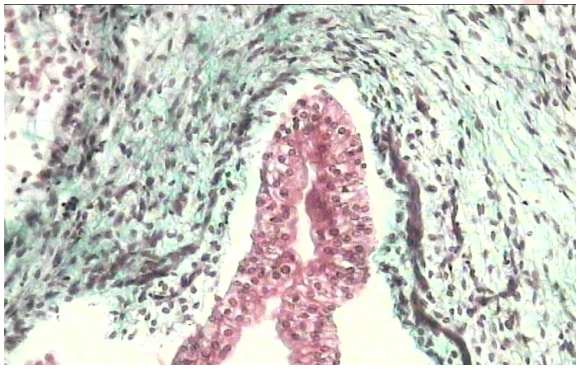
The mesenchymatous tissue surrounding the outer layer of metanephrogenic tissue differentiated into collagen fibrils and few fibroblasts with elongated oval nuclei running parallel to the long axis of the kidney (Fig 3). This is the anlage of future capsule.

Fig. 3: Depicts branching ampulla and developing capsule in 12 wks fetus in H&E X 10.



Cortex and medulla were not differentiated. Hilar region showed a larger pelvis with a small lumen lined by 2-3 layered thick epithelium having large rounded nuclei. Mesenchymal cells in the periphery were loosely arranged as compared to ones immediately surrounding the pelvis (Fig 4).

Fig-4: A section showing pelvis lined by 2-3 layered thick epithelium surrounded by thick mesenchyme in 12 wks fetus in Masson's trichrome X 10.

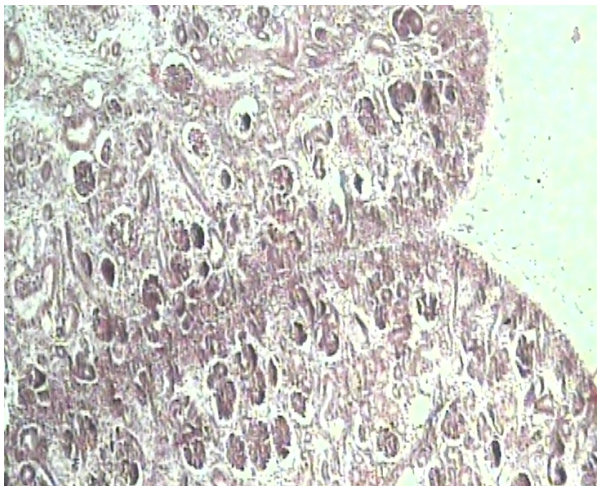


At 14 wks – zone of transition appeared b/w cortex and medulla. Here the pelvis was lined by same epithelium as in fetus of 12-13 wks but the mesenchyme surrounding it was more dense.

At 15 wks- well differentiated cortex and medulla were seen. Outermost zone of cortex was very darkly stained known as the neogenic zone. Neogenic zone contained many glomeruli along with PCT and DCT. Numerous collecting tubules lined by tall columnar cells were seen and the pelvis was multi layered epithelium.

GROUP 3 – 16 WKS TO 18 WKS: By 16 wks, kidney increased in size. Lobulation was still visible. Capsule was well differentiated with numerous collagen fibrils running parallel to the long axis of the kidney. Beneath the capsule many developing glomeruli were seen in the neogenic zone which were now compactly arranged due to decrease in the interstitial tissue. Another important finding in this group was that the parenchyma of the two adjacent lobules was separated by the neogenic zone. This zone is similar to the neogenic zone seen under the capsule and extends from the subcapsular area to the pelvis of the kidney. It gives the appearance of a column or septum and is known as the primary columna Bertini (Fig 5).This column marks the junction of primary lobules. Pelvis became extended and many minor calyces open into it. The epithelium lining the pelvis at this stage was multi-layered.

Fig. 5: Depicts Primary columna Bertini between 2 adjacent lobules in 16 wks fetus in Masson's trichrome X 4.



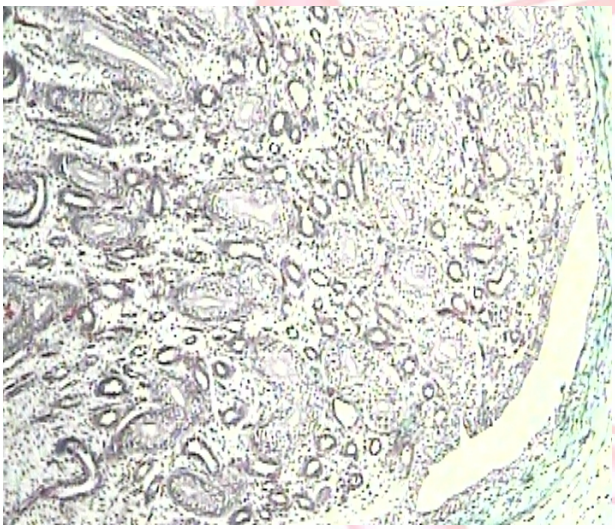
By 17 wks capsule became more thick and multilayered. Corticomedullary jxn are well defined. The most mature and larger glomeruli

are towards the juxta medullary region and the most immature are seen towards the periphery of the cortex.

Some of the collecting tubules showed stratification. Well defined arcades i.e many nephrons attached to a single collecting tubule, and pyramids were seen in the cortical region. Cone shaped pyramids were seen with apex towards pelvis and base towards cortex. Pelvis was lined by transitional epithelium.

By 18 wks –well defined pyramidal system was delineated. Minor calyx also appeared to be lined by transitional epithelium (Fig 6).

Fig. 6: Presence of Renal pyramid in 18 wks in Masson's trichrome X 4.



GROUP 4 – 19 WKS TO 22 WKS: Kidney size increased. Thick compact capsule was seen at periphery with increase in the collagen fibrils and cellular components. In the cortical region, the interstitial tissue had reduced to a minimum which has resulted in crowding of glomeruli. .

Arcade system was well developed .Within the cortex collecting tubules were seen aligning themselves in one direction from base of pyramid towards periphery of cortex. These regions were known as the medullary rays. In between two medullary rays, areas containing glomeruli along with convoluted tubules were seen known as the cortical labyrinth.

Majority of the collecting tubules appeared to be lined by stratified epithelium. Lobules were still in the process of fusion with the column of Bertini b/w them (Fig 7). Well developed transitional epithelium lined the pelvis (Fig 8).

Fig. 7: Primary columna Bertini in fetus of 22 wks in H&E X 4.

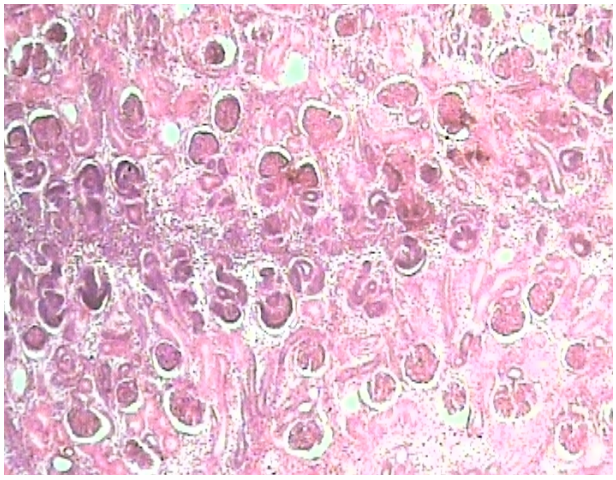
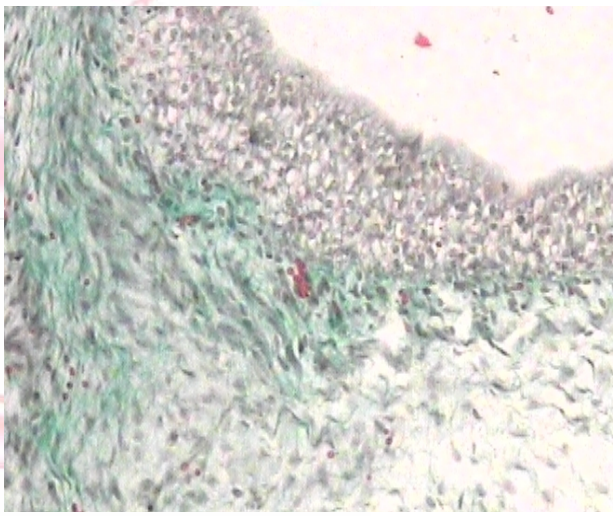
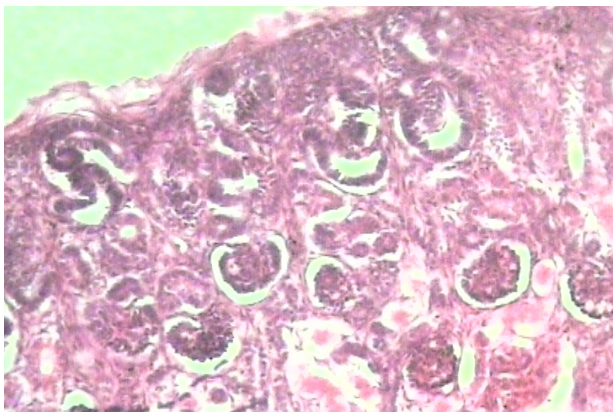


Fig. 8: Showing well defined transitional epithelium lining the pelvis in fetus of 22wks in Masson's trichrome X 40.



GROUP 5 – 23 WKS TO 34 WKS: Kidneys were larger with lobulation still present. The collagen fibrils within the capsule were arranged in wavy pattern. Almost negligible interstitial tissue was seen in the cortex. Subcapsular area or the neogenic zone showed metanephrogenic tissue (Fig 9).

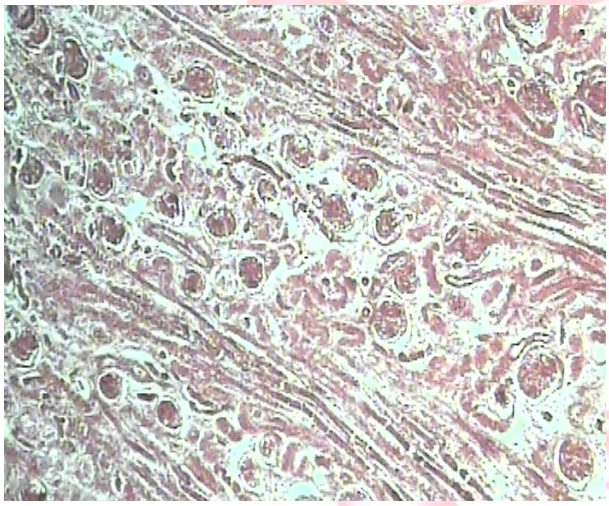
Fig. 9: Depicts almost negligible interstitial tissue in cortex of fetus of 23 wks in H&E X 10.



In the region of cortical labyrinth of cortex the most mature glomeruli were seen towards the medulla and most immature towards the capsule. Medullary rays were now composed of elongated collecting tubules (Fig 10).

In the longitudinal sections of kidney of this group, in between adjoining lobules, the primary columna Bertini was seen. This finding showed that the process of fusion of lobules was still going on. Pelvis was lined by transitional epithelium around which dense mesenchyme is seen.

Fig. 10: shows cortical labyrinth in between 2 medullary rays. Medullary rays comprising of elongated collecting tubules and Cortical labyrinth comprising of mature glomeruli in fetus28 wks in Masson's trichrome X 4.



DISCUSSION

Morphogenesis of human kidney begins at 5th week of gestation and extends upto the last month of third trimester of pregnancy [5]. Most of the results in the present study are in accordance with the previous authors while some are not. Thus, an attempt has been made to compare the findings of other authors with those made in this study.

In the present study, a very small undifferentiated kidney is seen at 10 weeks of gestation. In this kidney the development of pelvis is seen in the hilar region. This developing pelvis is in the form of a circular structure lined by a single layer of epithelium which is in accordance with Hamilton, Boyd and Mossman [5]and Osathanondh V and Potter, E. L, [2-4]. But, Sabita M et al [6] observed the developing pelvis at a little later stage of 14 weeks of gestation.

The renal pelvis appears to be lined by transitional epithelium by 18 weeks of gestation in consonance with Sabita M et al [6] who also observed that the pelvis is lined by transitional epithelium by 18-20 weeks of gestation.

The capsule of the kidney develops from the mesenchymatous tissue. This finding agrees with Huber, G.C [7] who also visualised that the mesenchymatous tissue is the anlage of the future capsule of the kidney.

In the present study, a zone of transition appeared between cortex and medulla at the starting of 14 weeks of gestation whereas Sabita M et al [6] observed this transitional zone at 16 weeks of gestation. Well differentiated cortex and medulla were first observed in this study by the end of 14 weeks of gestation. Hamilton, Boyd and Mossman [5] observed this differentiation between cortex and medulla by the end of 12 weeks of gestation. Sabita M et al found a well-differentiated cortex and medulla in a fetus of 18-20 weeks of gestational age.

Stratification of collecting tubules in the medullary region is observed by the 18th week of gestation, Sabita M et al [6] observed stratification of collecting tubules at 18-20 weeks of gestation.

In this study, renal pyramids and arcades appeared by 16-18 weeks of gestation in accordance with the previous observations made by Osathanondh, V and Potter, E.L [2-4] and Huber, G.C [7]. But, Sabita M et al [6] too observed them in their study by 18-20 weeks old fetus.

This study outlines the presence of lobulation at 10 weeks in utero till 33 weeks, which is in accordance with Osathanondh, V and Potter, E.L [2-4], Hamilton, Boyd and Mossman [5] and Sabita M et al [6]. Fusion of lobules is evident at 15 weeks of gestation. But Huber, G.C [7] observed fusion at 11 weeks of gestation. Sabita M et al [6] observed that the fusion of lobules occurs in a fetus of 16 weeks of gestation.

CONCLUSION

Pelvis develops in hilar region at 10 weeks of gestation and dilates to divide into major and minor calyces at 11 weeks and becomes lined by transitional epithelium by 18 to 20 weeks.

Lobulation of the kidney appears at 10 weeks and can be seen throughout the fetal life. Arcades system is observed at 16 to 18 weeks along with well defined pyramids.

In a 10 weeks old fetus, the kidney is in an undifferentiated form. There is a large amount of interstitial tissue in between the developing glomeruli and the collecting tubules in early stages of development but as the age advances there is decrease in this interstitial tissue which results in increased crowding of glomeruli and collecting tubules that in turn results in coiling of these tubules. A zone of transition appears between cortex and medulla at 14 weeks of gestation. Well-differentiated cortex containing large number of glomeruli, proximal convoluted tubules and distal convoluted tubules and medulla containing portions of collecting tubules and the loop of Henle, are seen in a fetus at the end of 14 weeks of gestation.

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Conflicts of Interests: **None**

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