

Histogenesis of Kidney in Human Fetuses

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Research Article

Abstract: The development of kidney is a very complex process having two parts, collecting part and excretory part. The collecting part develops from ureteric bud while excretory part develops from metanephric blastema. Information about development of kidney given in different text books of embryology does not include the details of microscopic appearance of various structures of kidney and its maturation at different gestational ages. The embryologists have not taken into account the histological details of various stages of glomerular development. The aborted human fetuses between 14- 40 weeks of gestational age with no obvious congenital anomalies were obtained. Kidneys were removed and histological slides of 7 microns were prepared and stained with Haematoxylin and Eosin method. The kidney lobules were observed at 14 weeks and after 18 weeks of gestation they disappeared. In the cortex, nephrogenic zone giving rise to new glomeruli was seen up to 37 weeks. Glomeruli passed through various stages of development. Proximal convoluted tubules and distal convoluted tubules were first identified at 20 weeks of gestation. Well differentiated medulla was seen after 24 weeks.

Keywords- Kidney, ureteric bud, metanephric blastema, cortex, nephrogenic zone, medulla.

1. Introduction:

Development of kidney has two parts, collecting part and excretory part. The collecting part develops from ureteric bud. The excretory part develops from metanephric blastema. Both these parts fuse with each other and the development is completed. Many varieties of cystic renal disease have been described. In most cases they result from failure of fusion between the tips of branches of ureteric diverticulum with the nephron, developed from metanephric blastema. So it is very essential to know the embryological details of kidney development to diagnose and treat such cases.

The description of development of kidney given in different text books of embryology does not include the details of microscopic appearance of various structures of kidney and its maturation at different gestational ages. The authors have not taken into account the histological details of various stages of glomerular development.

Due to recent advance in the medical field, it is now possible for the premature babies to survive successfully. For that it is essential to have knowledge regarding histological maturity of kidney and its functional status at the given gestational age. Hence the present study was undertaken to study in detail the appearance of various histological elements of kidney in relation with gestational age.

2. Material and Method:

Forty aborted human fetuses between 14- 40 weeks of gestational age with no obvious congenital anomalies were obtained from the Department of Obstetrics and Gynaecology, Government Medical College Miraj, with the prior permission of Head of Department and consent of parents. The study was approved by the Ethical Committee. Gestational age, sex, weight and crown- rump length were noted in detail. Kidneys were removed from the abdomen and sections of right and left kidneys were taken in such a way that they included cortex, medulla and hilum and were fixed in 10% formalin for 48-72 hours. The tissue was processed and paraffin blocks were prepared and 5-7 μ m in thick sections were taken on the rotary microtome. The slides were stained with haematoxylin and eosin and were observed under light microscope.

3. Observation:

The microscopic structure of kidney was studied by examining the slides under light microscope under low and high power after staining with haematoxylin-eosin stain. The observations made at different gestational ages were as follows-

3.1 At 14 weeks of gestation

On panoramic view, the kidney showed lobulation. In the superficial part of the cortex, just beneath the capsule, there was a zone of undifferentiated mesenchymal tissue having closely packed cells

(**Figure 1**). This was the nephrogenic zone containing nephrogenic cells. Beneath the nephrogenic zone, the growing ureteric bud in the form of ampulla was seen. (**Figure 2**) The cells of the ureteric bud were cuboidal with centrally placed nuclei. This bud was surrounded by group of nephrogenic cells which were forming a cap over the ampulla. At places it had divided dichotomously into two to form new tubule which were parallel to the surface of the kidney. Some cells were forming groups which were seen at an angle between the growing ampulla and old tubule.

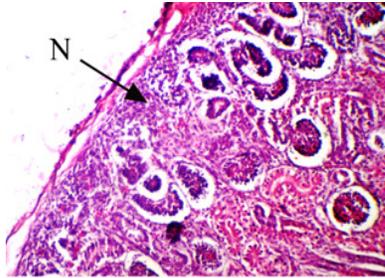


Figure 1-14 weeks, (10X)
N- Nephrogenic zone

Deep to the nephrogenic zone, but in the superficial part of the cortex, various stages of developing glomeruli were seen.

3.1.1 Stage I

In the superficial part of the cortex the ureteric buds were seen dividing. At the angle between the division and the old tubule, hollow structures lined by single layer of cells with oval nucleus having central cavity were seen. (**Figure 2**) These were nephrogenic vesicles which represent most primitive form of glomerulus.



Figure 2-14 weeks, (40 X)
V - Nephrogenic vesicle

3.1.2 Stage II

At places there were 'S' shaped hollow structure, with the cavity, lined by single layer of cells. They 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 portions having convex margin were lined by low cuboidal cells while the outer wall having concave margin were

lined by tall columnar cells having large oval nuclei. (**Figure 3**)

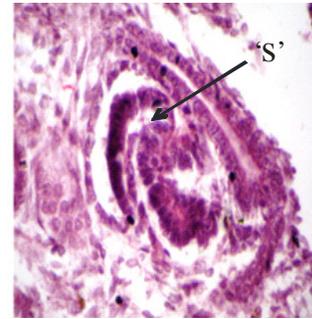


Figure 3-14 weeks, (40 X)
S - S shape glomerulus

3.1.3 Stage III

In some developing glomeruli, the lower portion of the 'S' tubule had become crescentic. 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 with very few capillary spaces lined by endothelial cells were seen. (**Figure 4**)

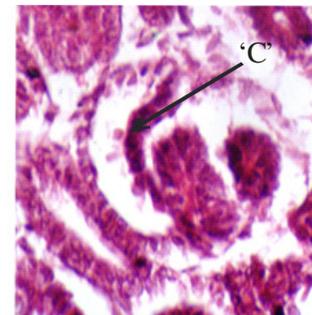


Figure 4-14 weeks, (40 X)
C - Crescentic glomerulus

3.1.4 Stage IV

In some 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. (**Figure 5**)



Figure 5-14 weeks, (40 X)
'Cp'- capillary invagination in crescent

3.1.5 Stage V

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. **(Figure 6)**

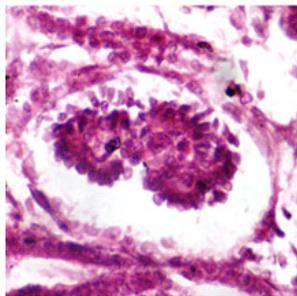


Figure 6-14 weeks,(40X)

3.1.6 Stage VI

The glomeruli present in the deeper aspects of the superficial cortex showed well marked lobulations. 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. **(Figure 7)**

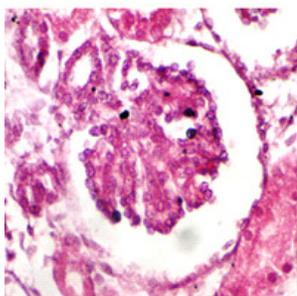


Figure 7-14 weeks,(40X)

3.1.7 Stage VII

In the deeper part of the cortex, the glomeruli were present in mature form. In the Bowman's capsule the network of glomerular capillaries was 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. **(Figure 8)**

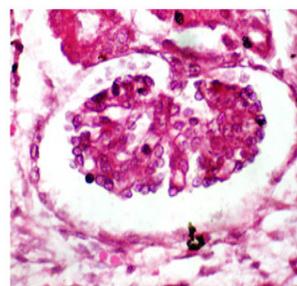


Figure 8-14 weeks,(40X)

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 the 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.

The medulla consisted of 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 RBCs were seen, scattered in the medulla.

3.2 At 18 weeks of gestation

Lobules appeared fused each other in section. The cortico medullary differentiation was better as compared to the previous stage. In medulla, irregular tubules of various dimensions, in between the connective tissue were seen. These were probably the collecting tubules. Few tubules of smaller dimension lined by simple cuboidal cells with eosinophilic cytoplasm and round nuclei are seen. These might be thick segments of the loop of Henle.

3.3 At 20 weeks of gestation

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 convoluted tubules and distal convoluted tubules with their characteristic staining pattern can be identified for the first time. **(Figure 9)**

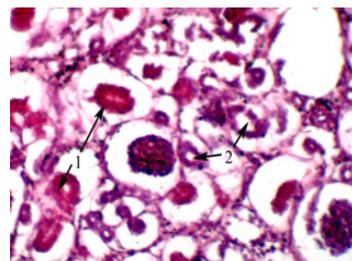


Figure 9-20 weeks,(40X)

1. Proximal convoluted tubule
2. Distal convoluted tubule

3.4 At 24 weeks of gestation

Cortico medullary differentiation had become more distinct. Cortex was increased in thickness. More

number of proximal convoluted tubules and distal convoluted tubules were identified with their characteristic staining pattern.

3.5 At 32 weeks of gestation

Beneath the capsule, nephrogenic zone was very thin and at places it was interrupted by the glomeruli. The mature glomeruli were observed in the superficial part of cortex, close to the nephrogenic zone. Very few immature developing glomeruli were seen scattered in the superficial cortex. (Figure 10)

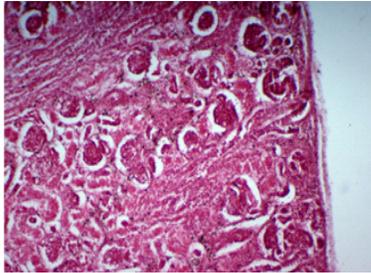


Figure 10 -32 weeks,(10X)

3.6 At 37- 40 weeks of gestation

Subcapsular nephrogenic zone disappeared. Well differentiated cortex and medulla were seen. The vascularity of both cortex and medulla was increased. Beneath the capsule there were glomeruli which showed lobulated glomerular tuft. As observed deeper in the cortex, more mature forms of glomeruli were seen. At the juxta medullary region few abnormally large glomeruli were seen. The medulla showed 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. (Figure 11)

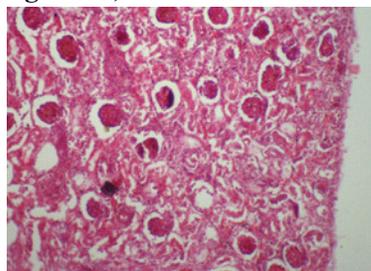


Figure 11 -38 weeks,(10X)

4. Discussion:

4.1 Kidney lobule

In present study, at 14 weeks of gestation, in histological sections, the kidney appeared in lobulated form. At 18 weeks of gestation the kidney showed lobulated appearance macroscopically but the lobules were fused in the histological sections.

Sabita Mishra, Anant Dinesh, J. M. Kaul¹ in their study observed that at 14 weeks, the kidney was in

lobulated form but at 16 weeks the lobules appeared to be fused.

4.2 Cortico Medullary Differentiation

At 24-26 weeks of gestation, Cortico medullary junction was well differentiated and it had become more distinct.

Sabita Mishra, Anant Dinesh, J. M. Kaul [1] have documented that, cortico-medullary junction was well defined at 18-20 weeks of gestation.

According to Helena Maria Lizardo-Daud[2], the corticomedullary differentiation is completed between 25-30 weeks.

4.3 Nephrogenic zone

In present study, from 14 weeks to 32 weeks the nephrogenic zone was observed beneath the capsule. At 14 weeks this zone became thick and formed a broad band beneath the capsule. Thereafter the thickness gradually decreased. After 22 weeks it was confined to a very thin strip beneath the capsule in the superficial cortex containing undifferentiated mesenchymal cells. Continuous nephrogenic zone was seen up to 32 weeks of gestation; thereafter it became discontinuous and interrupted at places by the developing renal corpuscles but can be seen up to 36 weeks of gestation. The nephrogenic zone was not seen after 38 weeks.

The findings in present study were well correlated with the findings of Morag Mac Donald and John Emery [3]. Potter [4] had said that nephrogenic zone was seen only up to 32 to 34 weeks of gestation.

4.4 Ampullary growth

At places ampulla had divided dichotomously into two and produced next generations of tubules which were parallel to the surface of the kidney. Edith Potter [4], in his study had also observed similar ampullary growth. He had quoted that the ampulla divides dichotomously parallel to the kidney surface.

4.5 Renal corpuscles

In present study various stages of glomerular development were seen. These were as follows-

In **Stage I** it was in the form of Vesicle, in **Stage II** it was 'S' shape, in **Stage III** it was crescentic form, in **Stage IV** the developing capillaries were invaginated in the crescent, in **Stage V** The capillaries in the Bowman's capsule showed lobulations, in **Stage VI** there was well marked lobulation in the capillaries and **Stage VII** were mature glomeruli.

Edith Potter [4], John Emery and Morag Macdonald [5], Kei Takano, Kawasaki, Imizumi [6] had described various stages of glomerular development in their study which were comparable with present study.

The initial stages of developing glomeruli (stage I to stage IV) were seen in the superficial part of cortex. The

later stages of developing glomeruli (stage V to stage VII) were present in deeper part of cortex. The vesicular form of glomeruli was most superficial in the cortex, just beneath the nephrogenic zone. These vesicles were located at the angle between the division of ampulla and old tubule. As we go deeper in the cortex the mature forms were seen. The most mature glomeruli were present in deeper cortex, close to medulla.

Arne Ljungqvist [7] had documented the same findings in their study.

4.6 Tubules in the cortex

In present study, at 14 weeks, the tubules in cortex were in developing phase and cannot be differentiated into proximal convoluted tubule or distal convoluted tubule. Proximal convoluted tubule and distal convoluted tubule, with their characteristic staining pattern, were identified at 20 weeks of gestation. Then 20 weeks onwards, they were constantly seen and they became well differentiated. They were better identified in the deeper part of cortex. Their number increased with increasing gestational age.

Sabita Mishra, Anant Dinesh, J. M. Kaul [1] had quoted that at 22 weeks, two types of tubules with different staining pattern, one deeply eosinophilic with small lumen and the other deeply basophilic were observed.

4.7 Medulla Of kidney

In present study, medulla of kidney at 14 weeks of gestation was in primitive form. At 20 weeks, in addition to collecting tubules, thick and thin segments of loop of Henle were identified. The vascularity of the medulla also increased. At 24 weeks, in the sections, in deeper part of medulla, the collecting tubules were lined by columnar cells with basal nuclei. These were the ducts of Bellini. From 24 weeks onwards, the number of well differentiated tubules went on increasing while the connective tissue was decreasing in amount. Not much emphasis had been given regarding development of medulla, in the earlier studies. Sabita Mishra, Anant Dinesh, J. M. Kaul [1] had quoted that at 22 weeks the medulla appears more mature.

But none of the earlier studies had elaborated the sequence of maturation of medulla with the increasing gestational age and the period of appearance of collecting tubules and thick and thin segments of loop of Henle and ducts of Bellini.

5. Conclusion:

- [1] The kidney lobules were fused completely at 18 weeks in histological sections.
- [2] The nephrogenic tissue, giving rise to new nephron, was seen up to 36 weeks. So new renal corpuscles were formed up to 36 weeks. Thereafter the corpuscles only mature.

- [3] The glomeruli passed through various stages of development from vesicular form to mature form. The primitive forms of glomeruli were seen in the superficial part of cortex. As they matured, they moved towards the medulla. The most mature glomeruli were seen in the deeper part of cortex close to medulla.
- [4] The proximal and distal convoluted tubules were identified in cortex after 20 weeks of gestation.
- [5] The medulla became well differentiated at 24 weeks of gestation.

6. Bibliography:

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