Original Research Article

Histological differentiation of human fetal kidney

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International Archives of Integrated Medicine, Vol. 2, Issue 7, July, 2015.

Available online at http://iaimjournal.com/

ISSN: 2394-0026 (P) **ISSN: 2394-0034 (O)**

Received on: 22-06-2015 **Accepted on:** 28-06-2015

Source of support: Nil **Conflict of interest:** None declared.

Abstract

Introduction: The description of development of human kidney given in various textbooks doesn't include detail microscopic appearance of kidney at various fetal ages. So an attempt was made in this study to gather information on this topic.

Material and methods: The present study was carried out on 15 human fetuses of known gestational age (GA). The sections of kidney were processed and were stained using Hematoxylin and Eosin.

Results: At 12th week of GA various stages of developing glomeruli were observed in the substance of the kidneys. In the cortex, various cut sections of the tubules were observed without any differentiation as proximal (PCT) and distal tubules (DCT). The second trimester section showed well differentiated the PCT and DCT by 16th week. Distinct brush border was observed in PCT by the 16th week. Immature duct system was observed in the medulla. The nephrogenic zone was appreciated till 36 weeks. By 28th week the sections of DCT were observed adjacent to the renal corpuscles indicating the developing juxtaglomerular apparatus.

Conclusion: As it is essential to know the developmental morphology of kidney, the present study explains every component of it in detail.

Key words

Glomeruli, Proximal convoluted tubule, Loop of Henle, Histogenesis.

Introduction

Prenatal period is a very crucial 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 fetal

kidney has about 12 lobes but these are fused in adults to present a smooth surface [1].

Kidneys develop in the intermediate mesoderm in the cranio-caudal direction. They develop in pronephric, mesonephric and metanephric stages. The development of the kidneys illustrates the famous dictum by Haeckel that 'ontogeny recapitulates phylogeny'. This means that the development of the three kidney types follow an evolutionary pattern. The development of kidney is a very complex process having two parts, collecting and excretory parts. The collecting part develops from ureteric bud while the excretory part develops from metanephric blastema [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 7^{th} week in relation to 6^{th} division of ureteric bud [3]. 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 [4].

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 (GA). Hence the present study was undertaken to study in detail the appearance of various histological elements of kidney in relation with GA. The description of development of human kidney given in various textbooks doesn't include detail microscopic appearance of kidney at various fetal ages. So an attempt was made in this study to gather information on this topic.

Material and methods

The present study was carried out on 15 formalin fixed human fetuses (3 first trimester, 6 second trimester and 6 third trimester) of known GA in the department of Anatomy, Kasturba Medical College, Manipal. The spontaneously aborted and stillborn fetuses were procured from the department of Obstetrics and Gynecology, Kasturba Hospital, Manipal after taking informed consent for museum specimen preparation. The GA of first trimester fetuses ranged from 10 to 12 weeks whereas it ranged 16 to 24 weeks and 28 to 36 weeks for the second and third trimesters respectively. Fetuses with any external deformity were excluded from the study. A vertical incision was made on the abdomen and the kidneys were resected and the sections were taken including both the cortex and medulla. The tissues were processed for histological observations. The slides were stained using Hematoxylin and Eosin and were observed under light microscope.

Results

The microscopic anatomy of the kidneys was observed at different GA and the changes were noted. The various components showed maturation at different GA. The detailed microstructure of the kidney is described according to the three trimesters.

First trimester: (10 to 12 weeks)

In the first trimester the cortex and medulla did not show distinct differentiation until 12^{th} week. The section of kidney when observed under 10X (**Figure - 1a**) displayed a thick nephrogenic zone containing clusters of mesenchymal cells deep to the capsule. At 12^{th} week of GA various stages of developing glomeruli were observed in the substance of the kidney interspersed with undifferentiated mesenchymal cells as shown in **Figure - 2**. There were hollow structures lined by cuboidal cells adjacent to the capsule indicating the nephrogenic vesicles. Some of the glomeruli appeared 'S' shaped containing clusters of cuboidal to columnar cells without any network of capillaries. The crescentic shape was observed

to be the next stage of development, where the crescent was lined by cuboidal cells which were invaginated by the mesenchymal cells. The juxtamedullary glomeruli showed the further signs of maturity by developing blood capillary network and flattening of the lining of Bowman's capsule.

Figure - 1: Kidney under 10X showing cortex and medulla (Hematoxylin and Eosin).
Figure - 1a: First trimester kidney,
Figure - 1b: At second trimester
(1-Nephrogenic zone, 2- Developing glomerulus)

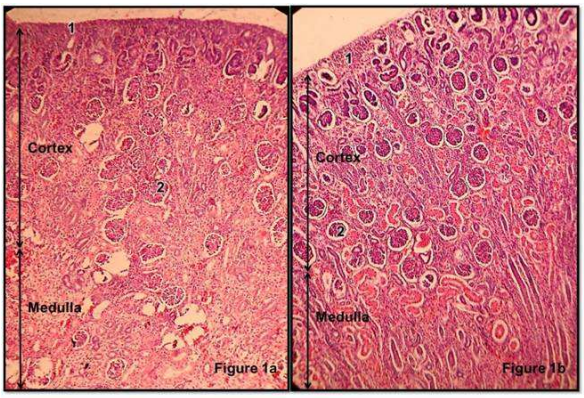
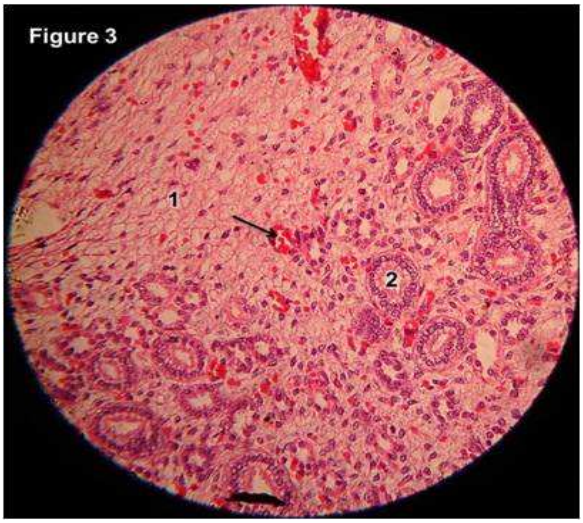


Figure - 2: Kidney; cortex under 40X (Hematoxylin and Eosin) showing various stages of glomerular development, Nephrogenic zone (black arrow) and cut sections of tubules (green arrow).
(1-Nephrogenic vesicle, 2- 'S' shaped glomerulus, 3- Crescentic glomerulus, 4- Mature glomerulus.)

In the cortex, various cut sections of the tubules were observed without any differentiation as proximal (PCT) and distal tubules (DCT). The tubules were lined by simple cuboidal cells without any surface modifications.

The medulla in the first trimester showed the sections of tubules with cuboidal cells without any distinct blood vessels. Clusters of mesenchymal cells were observed between the tubules (**Figure - 3**).

Figure - 3: Kidney; medulla under 40X (Hematoxylin and Eosin).
1-Undifferentiated mesenchymal cells, 2- Cut sections of collecting tubules, developing capillaries (black arrow)



Second trimester: (16 to 24 weeks)
When observed under low magnification (**Figure - 1b**), the thicker cortex and thinner medulla were differentiated by a distinct corticomedullary junction by 16th week of GA. The nephrogenic zone was observed under the capsule. The mature renal corpuscles were observed by 20th week with well differentiated Bowman's capsule and tuft of glomeruli within it. In the cortex, the tubules were differentiated by 16th week as PCT and DCT. Distinct brush border was observed in PCT by the 16th week.

Immature duct system was observed in the medulla with the cut sections of collecting

tubules which were lined by columnar to cuboidal cells. The thick and thin segments of Loop of Henle were not differentiated till 24th week.

Third trimester: (28 to 36 weeks)

The nephrogenic zone was appreciated till 36 weeks. The cortex and medulla were distinctly differentiated at this stage. Mature renal corpuscles were observed in the cortex (**Figure - 4**). By 28th week the sections of DCT were observed adjacent to the renal corpuscles indicating the developing juxta glomerular apparatus (JGA) (**Figure - 5a**). The thin and thick segments of loop of Henle were identified by 28th week (**Figure - 5b**).

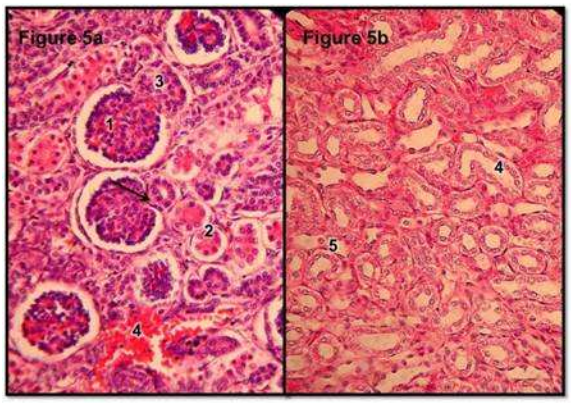
Figure - 4: Kidney under 10X showing cortex and medulla at third trimester. (Hematoxylin and Eosin).
(1-Capsule, 2- Glomeruli)

Discussion

According to Maria et al nephrogenesis in human starts at 6th week of intrauterine life and is completed by 35th week of gestation. They also state that distinct corticomedullary differentiation is observed at 25 weeks. The differentiation of tubules was observed during 25 to 30 weeks of gestation [2]. In the present study the differentiation of tubules was observed as early as 16th week of gestation.

According to Sadiqali, et al. at 14 weeks of gestation the section of kidney showed a nephrogenic zone containing undifferentiated mesenchymal cells just underneath the capsule which decreased in thickness by 32 weeks. The authors also described the various stages of developing glomeruli. By 24 weeks the cortico medullary differentiation had become more distinct. By 40 weeks subcapsular nephrogenic zone disappeared [5]. The findings of present study were in agreement with the above author.

Figure - 5: Kidney; under 40X (Hematoxylin and Eosin)
Figure - 5a: Cortex
(1-Glomerulus, 2- PCT, 3- DCT, 4- Capillary, Site of developing Juxtaglomerular apparatus)
Figure - 5b: Medulla
(4-Collecting tubule, 5- Thin limb of loop of Henle)



According to Tank, et al. at 12 weeks the kidney was covered by a thin capsule with an undifferentiated corticomedullary junction. In the cortex the immature developing glomeruli were more in number. At higher magnification the PCT and DCT can be easily identified by 17 weeks. In the medulla, the cells were arranged in groups indicating the formation of collecting tubules. The loops of Henle were differentiated by 17 weeks. The primitive blood vessels were lined by simple squamous epithelium [3]. In the present study the differentiation of tubules in the cortex was observed as early as 16th week and the medulla started differentiating by 28 weeks where the loops of Henle were identified.

According to Daković-Bjelaković, et al. 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 [6].

Few authors have mentioned that the nephrogenic zone disappears by 36th week [3, 7, 8]. In the present study the nephrogenic zone was observed till 36 weeks.

According to Emery, et al. the scattered glomeruli were found in two zones; one near the arcuate vessels and the other near the capsule. It was suggested that the scattered glomeruli in the arcuate vessels represent involution forms of large glomeruli. They also describe that the 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 [9]. In the present study as the arcuate vessels were not identified, the above findings could not be substantiated.

Study by Bello, et al. on histological differentiation of bovine kidney in first trimester kidney showed numerous mesenchymal cells with few developing glomerulus. In the medulla few types of collagen fibers were seen. In second trimester fully formed glomeruli were formed moderate number of mesenchymal cells and immature developing duct systems were seen. In third trimester numerous developed glomeruli with mature duct system were seen [10]. The findings were similar to that of the present study indicating similarities in histogenesis of kidneys in bovine and in human fetuses.

According to Mishra S, et al. the cortico-medullary junction was well defined at 18-20 weeks of gestation [11]. According to Maria H et al the corticomedullary differentiation is completed between 25-30 weeks [2]. Similar findings were observed in the present study.

The lack of availability of fetuses of all weeks of gestation was a limitation as it would be possible to explain the developmental process more accurately. Also the vascular development was not considered in detail in the present study.

Conclusion

As it is essential to understand the developmental morphology of kidney, the present study explains it in detail. More emphasis is given to the development of each component especially the appearance of JGA which is been not explained previously.

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