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Morphogenesis of Rabbit Kidney Pre-and Postnatal

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Key words

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ABSTRACT:

Mammalian renal development differs from that of most of the other organs in that it proceeds through a series of three successive phases, each is marked by the formation of a more complex pair of kidneys. These kidneys are called the pronephros, mesonephros, and metanephros. The current study has been conducted to elucidate the developmental changes of rabbit kidneys during their pre- and postnatal life. In the present study we used samples, at different ages, of the rabbit kidneys from embryonic day 15 (E15) till maturity for light and scanning electron microscopical investigation. At E15, large mesonephros, occupied a great part of abdominal cavity of rabbit embryo, and undifferentiated metanephros were noticed. At E19 metanephros became differentiated into cortex and medulla with the initiation of nephron-forming stage. Additionally at this stage, the caudal series of mesonephros still detected but in degenerated and atrophied structure. Just before birth, at E30, the kidney demonstrated well-developed renal corpuscles, differentiated proximal and distal convoluted tubules, with apparently detectable loop of Henle and large collecting ducts. Shortly after birth rabbit kidney showed further morphogenesis and at two-months old, the kidney of rabbit with mature histological structure of the renal parenchyma was documented. In conclusion, the development of rabbit kidneys occurred mainly during the prenatal period while their histological maturity occurred from two to three weeks after birth. The present findings were discussed with previous publications.

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1. INTRODUCTION

Morphogenesis of the mesonephric nephron starts with the formation of mesenchymal condensates, which soon develop into renal vesicles and S-shaped bodies. Similar developmental events were noticed in the metanephros. However some definite, mainly ultrastructural, differences between the two have been observed in a mature nephron (Tiedemann, 1976, 1983; Tiedemann and Wettstein, 1980; Schiller and Tiedemann, 1981; Tiedemann and Zaar, 1983). There was great difference in size, distribution, and functional maturity of the mesonephric nephrons between the different species (Friebova and Goncharevskaya, 1982).

The mammalian kidney develops as the product of inductive interactions between the ureteric bud (UB) and the adjacent metanephric mesenchyme (MM). The first stage in nephrogenesis is the condensation of patches of induced MM to form renal aggregates (Stark et al., 1994; Majumdar et al., 2003; Carroll et al., 2005; Bridgewater et al., 2008). The adult kidney consists of a large number of specialized epithelial, stromal, and endothelial cells. Renal epithelial and stromal cells share a common lineage that is specified early in development, but diverges once kidney development proceeds. In mammals, this lineage is apparent shortly after gastrulation in a region of mesoderm, called the intermediate mesoderm. Moreover, the kidney develops along the antero-posterior (AP) axis in a temporal sequence. Early anterior kidney structures include the pronephros and mesonephros, whose complexity, size, and duration

vary greatly among vertebrate species. In the mouse, the pronephros is barely detectable, whereas mesonephric tubules are well developed with a proximal glomerulus and convoluted tubules that empty into the nephric duct. The adult, or metanephric, kidney forms at the posterior end of this intermediate mesoderm. Thus, the intermediate mesoderm requires both medio-lateral patterning and AP patterning signals to determine the adult kidney field (Patel and Dressler, 2013).

The origin of the different segments of the nephron is of mesenchymal origin while the collecting duct is derived from the Wolffian duct (Hamilton 1952). Development of the metanephros begins during fetal life but is only completed after birth. All the nephrons do not develop at the same time. The first nephrogenic masses appear under the kidney capsule and are progressively differentiated and connected to the collecting tubules; new nephron generations are formed at the periphery of the kidney so that, at any time of fetal life, the most differentiated ones will be the most deeply embedded. At birth, most nephrons appear as mature formations but in certain species, particularly in the rat, some nephrogenic masses can still be seen, their differentiation being achieved several days or weeks following birth (Kasimierczak, 1971 and 1976; Larsson 1975). Since, the development of rabbit kidneys is not studied well, at least recently. So the current study was conducted to through some highlights on the morphological aspects of the rabbit kidneys during the pre- and postnatal life.

2. MATERIAL AND METHODS

Embryos, fetuses, newborn and adult V-line white rabbits were obtained from the farm of Faculty of Agriculture, Alexandria University, Egypt. The rabbits were housed in separate cages with 12 hour light/12 hour dark cycles and allowed free access to water and rations. The age of fetuses and rabbits was estimated according to the records of the farm. Prenatally, the day of mating was considered the day one of embryonic life while the day of delivery was considered the day one of postnatal life.

2.1. Light microscopic examination

The pregnant female rabbits, at different stages of pregnancy starting from the E15, 19, 21, 25, 30, were slaughtered and the embryos and fetuses were removed, three embryos in each age (n=15). In case of fetuses under E21, the whole fetuses were fixed in 10% neutral buffered formalin (for 2-5 days) and Bouin's solution (for 24-48 hours). In case of older fetuses, newborn and adult rabbits, samples from the kidneys were dissected out after incision of the abdominal wall and were preserved in the same fixatives for the same periods. The kidney samples were then dehydrated in ascending grades of ethanol, cleared in xylene, impregnated with melted paraffin wax. Finally paraffin blocks of the processed samples were prepared. Thin sections (5-7 µm thick) were cut and mounted on egg albumin-glycerin coated glass slides, dried in an electrical incubator for 30-60 minutes and stained with the following stains, according to Bancroft and Gamble (2008).

- Hematoxylin and eosin (H and E) for general inspection of the organs.
- Gomori's reticulin method for detection of reticular fibers.
- Masson's trichrome technique for demonstration of collagen fibers and smooth muscles.
- Periodic Acid Schiff reaction (PAS) for detection of glycoproteins.
- Combination of PAS and Alcian blue (AB) for the demonstration of the mucins and acid mucins.

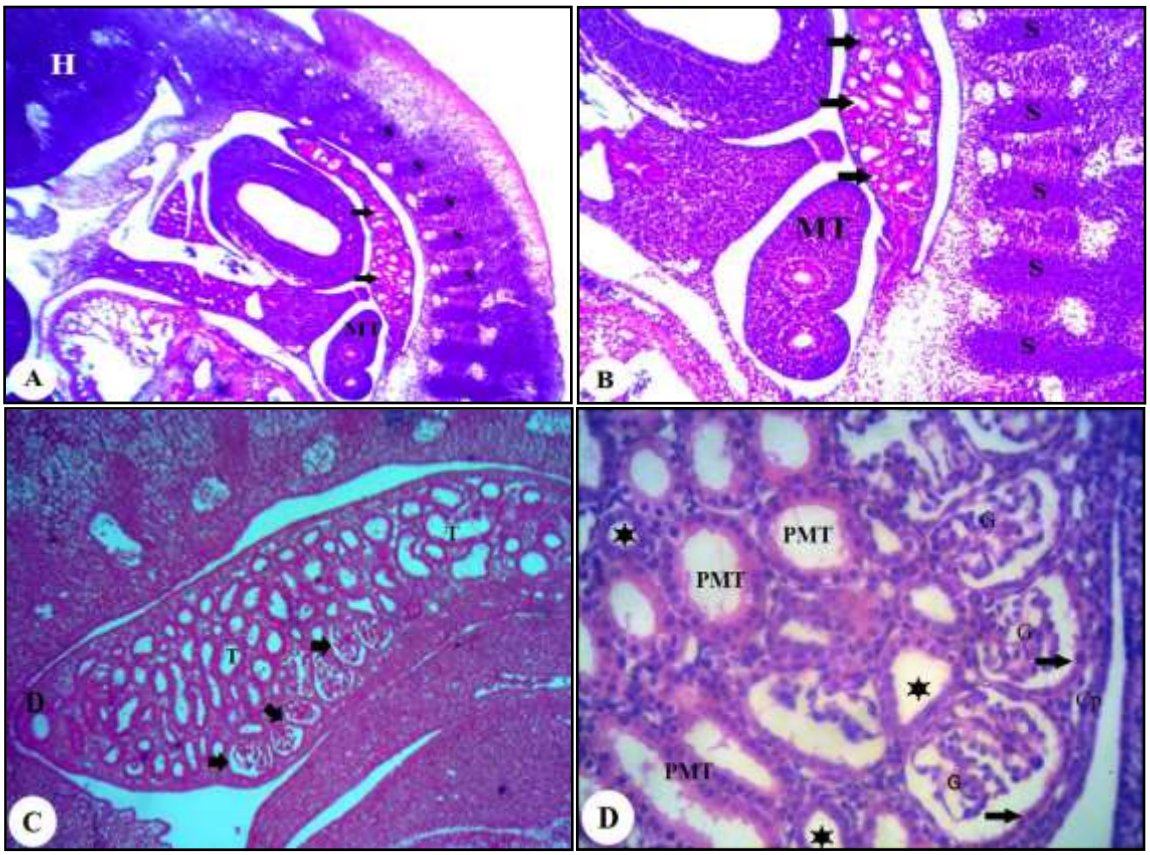
2.2. Scanning electron microscopic (SEM) examination

Samples from the kidneys of fetuses at E19, E25, and E30 and from rabbit aged one and two weeks and two months were used for SEM examination according to Echlin (2009). The samples were immediately immersed in 4F1G (2% formaldehyde, 1.25%glutaraldehyde in 0.1 M sodium cacodylate buffer) fixative at pH 7.2 and stored at 4°C. The fixed samples were washed in 0.1 M cacodylate buffer containing 5%sucrose processed through tannic acid, dehydrated in graded ethanol series for 15 minutes in each of 50%, 70%, 80%, 90% and absolute alcohol. The critical point dried samples (with carbon dioxide) were then attached to stubs with colloidal carbon and coated with gold palladium in sputtering device. The samples were examined and photographed with JEOL SEM 5300 operating 15Kv in the Faculty of Science, Alexandria University, Alexandria, Egypt.

3. RESULTS

As early as E15, both large mesonephros, occupied a great part of abdominal cavity of rabbit embryo, and undifferentiated metanephros were noticed (Fig. 1A). Mesonephros extended cranio-caudally approximately under and parallel to the somites of vertebral column and the primitive metanephros consisted of the outer

metanephrogenic mass (intermediate mesoderm) that surrounded the terminal part of the branched ureteric bud (Fig. 1B). Structurally the parenchyma of the mesonephros could not be divided into cortex and medulla and it consisted of mesonephric duct, lined by cuboidal epithelium, and a several series of mesonephric tubules and renal corpuscles. The tubules were divided into blind end forming renal corpuscle, proximal part and the distal part that terminated into the mesonephric duct (Fig. 1C). The blind end of the mesonephric tubules invaginated by a tuft of blood capillaries (glomerulus) to form double-layered renal capsules. The parietal layer of renal capsule was lined by low cuboidal cells while its visceral layer was lined by squamous cells. The rest of the tubules were divided into proximal segment toward the corpuscle, lined with more eosinophilic columnar epithelium, and distal segment lined with cuboidal epithelium and opened into the mesonephric duct (Fig. 1D). The intertubular spaces were filled by little amount of vascular mesenchymal tissue. The rabbit mesonephric nephron was structurally similar to the adult metanephrogenic nephron; however, the loop of Henle was absent. At the age of E19, the metanephros kidney of rabbit was demarcated in caudal region of abdominal cavity together with late stages of the degenerated mesonephros (Fig. 2A). At this developmental stage the parenchyma of the metanephros was differentiated into outer cortex and inner medulla. Within the developing cortex the metanephrogenic mesoderm started to form several solid and canalized renal vesicles.



1. Photomicrograph of rabbit kidney at E15. A; sagittal section showing the mesonephros (arrows) occupied large part of abdominal cavity under the somite (s) and metanephros (MT) located beside it. B; showing mesonephros (arrows) and metanephros (MT) together with the somites (S) at higher power. C; showing the mesonephros with its tubules (T) and corpuscles (arrows) caudally and mesonephric duct (D) cranially. D; showing glomeruli (G) of mesonephros at different stages of development with parietal layer of low cuboidal epithelium (arrows). The distal segments of mesonephric tubules lined by single layer of cuboidal cells (asterisk) and proximal segments of mesonephric tubules (PMT) lined by columnar cells. The capsule (Cp) formed of mesenchymal tissue. H&E X4 in A and X10 in B, X10 in C and X40 in D

The latter vesicle become elongated tubules and differentiated into the developing nephron and the most advanced one was observed at the corticomedullary junction while the new one appear at

the outer part of the cortex. One end of elongated metanephrogenic tubules became funnel shape forming the renal corpuscle that surrounded a tuft of capillaries (glomerulus) (Fig. 2B). The firstly developed nephron at the corticomedullary junction showed nearly mature nephron structures where it can be demarcated into renal corpuscle with its glomerulus, proximal convoluted tubules, distal convoluted tubules and loop of Henle (Fig. 2C). The developing medulla showed intensive undifferentiated mesenchymal tissue surrounded the newly formed collecting tubules; the latter tubules were lined by columnar epithelium. The outer part of metanephrogenic mass was arranged as sheath of two layers of flat cells that was considered the first step of kidney capsule development. SEM of this age confirmed the light microscopy where the parenchyma of metanephros kidney was divided into cortex and medulla. The medulla had the collecting tubules within intensive undifferentiated mesenchyme. The cortex had different stages and shapes of nephron development (Fig. 2D).

Also in this stage the mesonephros can be still detected however, in atrophied and degenerated nature where moderate atrophy was shown on the mesonephric tubules and glomeruli. The mesonephric capsules were condensed, the glomeruli were decreased in size, the intertubular connective tissue was increased and some of mesonephric tubules were collapsed. Some collapsed mesonephric tubules were lined with very low cuboidal cells. Sometimes there was vacuolization of the mesonephric glomeruli and the renal space increased in width.

At E25, the metanephros of rabbit showed a clear demarcation of cortex and medulla (Fig. 3A). In the cortex, the newly formed nephrons were concentrated and more numerous at the peripheral part of the cortex (outer cortex) whereas the earliest formed nephrons were less numerous and deeply located (juxtamedullary). There were numerous tubules of different wall thickness and luminal width (Fig. 3B). The medulla pointed towards the hilum and the pyramid proper was a projection of the central part of the medulla, and has the form of a cone considerably flattened (ventro-dorsally). Columnar epithelium covered the apex of medullary pyramids at the renal papilla while single layer of columnar epithelium with central nuclei lined the collecting ducts that had a wide lumen. Cell boundaries are normally clearly defined compared with the cells of the proximal and distal convoluted tubules. The terminal portion of these tubules is lined by a columnar epithelium and is called the papillary duct (Fig. 3C). There was a little and delicate intertubular and capsular connective tissue formed mainly of reticular fibers (Fig. 3D).

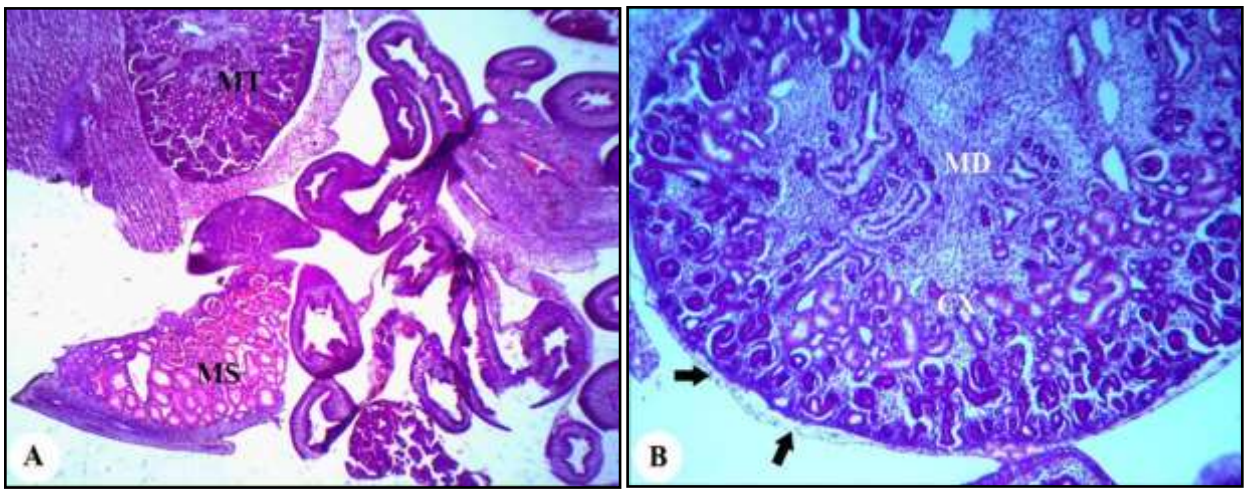


Figure 2

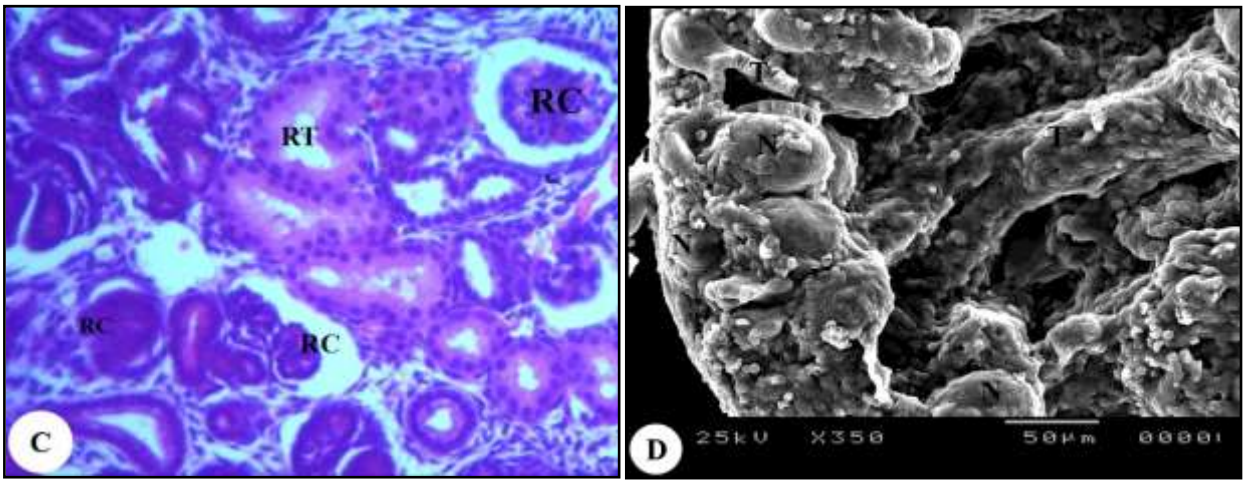


Figure 2. Photomicrograph of rabbit kidney at E19 A; the metanephros (MT0 and mesonephros (MS). B; showing the metanephric divided into cortex (CX), with nephrons and tubule at different stages of development, and medulla (MD) with large ducts. The capsule of metanephros consisted of two layers of cells. C; higher power of metanephros showing the renal corpuscles (RC) and renal tubules (RT). D; SEM of metanephros showing the developing nephrons (N) and tubules (T). H&E X4 in A, X10 in B and X40 in C

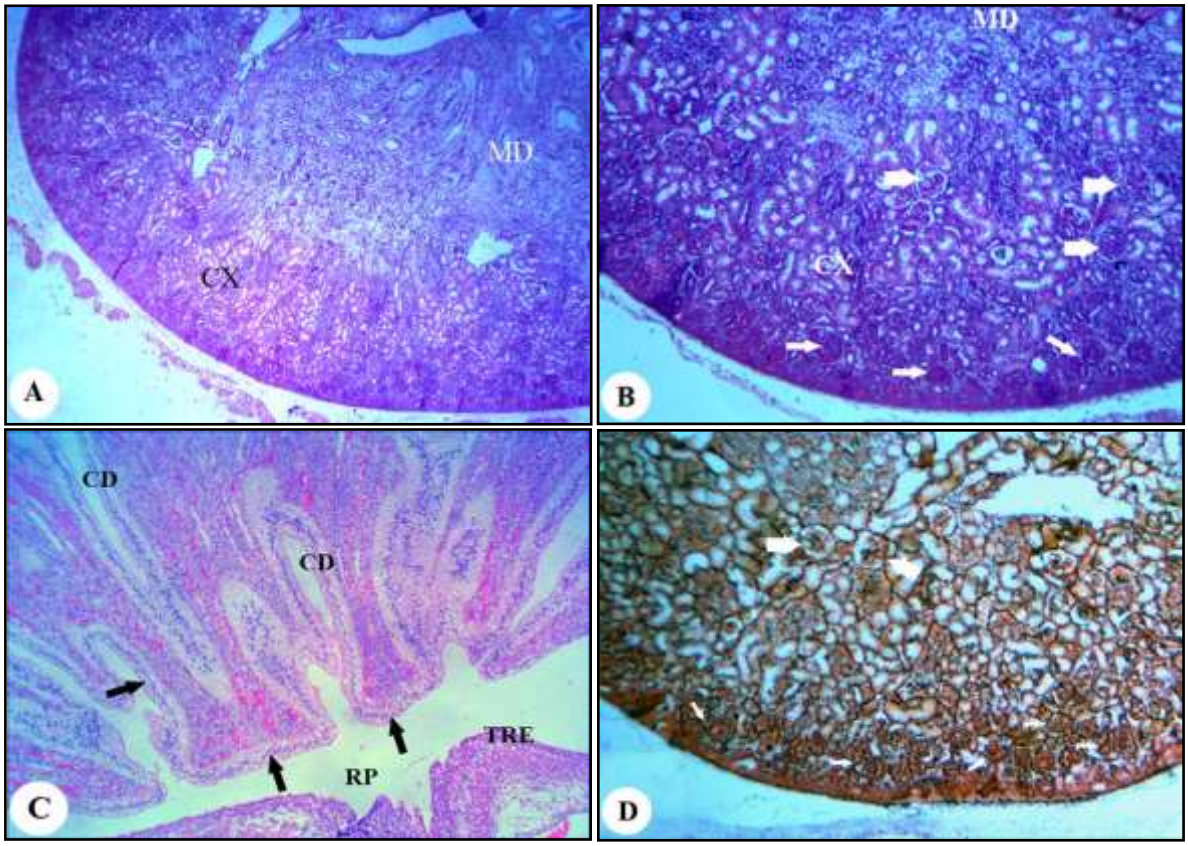


Figure 3. Photomicrograph of rabbit kidney at E25. A; the cortex (CX) and medulla (MD) well demarcated. B; the renal cortex (CX) contained the newly developed renal corpuscles (small arrows) in the outer region and the old ones (broad arrows) in the deep region. C; the renal medulla had collecting ducts (CD) and tubules and the renal papilla covered by columnar epithelium (arrows) while the renal pelvis lined by transitional epithelium (TRE). D; the developing reticular fibers in the capsule and intertubular spaces; note the newly developing renal corpuscles (small arrows) were more numerous at the outer cortex and the old one (broad arrows) near the medulla. H&E and X4 (A), X10 (B), X40 (C) and Gomori stain X10 (D)

By SEM the glomerulus located subcapsular with different stages of development and the glomerulus appeared to be invaginated in the Bowman's capsule. The Bowman's space appeared with different width. The cell bodies of podocytes were setting on the loops of blood capillaries and entirely covered them (Figure 4).

By the end of gestation period (E30) the renal cortex showed clear differentiated of the PCT and DCT with apparently detected loop of Henle. PCT was lined by high cuboidal acidophilic epithelium with clear brush border while DCT lined by low cuboidal less acidophilic epithelium with ill-defined brush border. In addition, the renal corpuscles were observed with narrow space between the parietal and visceral layers of Bowman's capsule (Fig. 5A). The renal medulla showed large collecting ducts, lined by a layer of high columnar epithelium, collecting tubules, descending and ascending limbs of renal loops (Fig. 5B).

The SEM showed the differentiation of the cortex and medulla (Fig. 5C). In the cortex the nephron with its different segments, the glomerulus invaginated the Bowman's capsule and the surface of the cell bodies of the podocytes were almost rounded and covered the glomerular capillaries entirely. The renal medulla showed longitudinally arranged renal tubules (Fig. 5D).

Postnatally and at one week old the kidney increased in size. In the renal cortex the rate of development was speeder at the periphery than the mid-cortical and subcortical zones with variation of the glomerular condensation from the cortical to the subcortical zones. The renal corpuscles were numerously detected at the cortical, subcortical than at juxtamedullary zones of the kidney. The corpuscles showed distinct Bowman's capsules with clear parietal squamous layer. Also PCT and DCT were more developed (Fig. 6A). The medulla in this age showed the collecting duct lined by cuboidal epithelium with clear intercellular membranes with faintly stained cytoplasm and centrally situated nuclei (Fig. 6B). PAS-alcian blue combination showed the well developed brush border of PCT (Fig. 6C). By SEM the renal corpuscle with space surrounding the glomerulus, several cells bodies of podocytes are seen closely gathered and the podocyte primary processes appeared covering the glomerular capillaries (Fig. 6D).

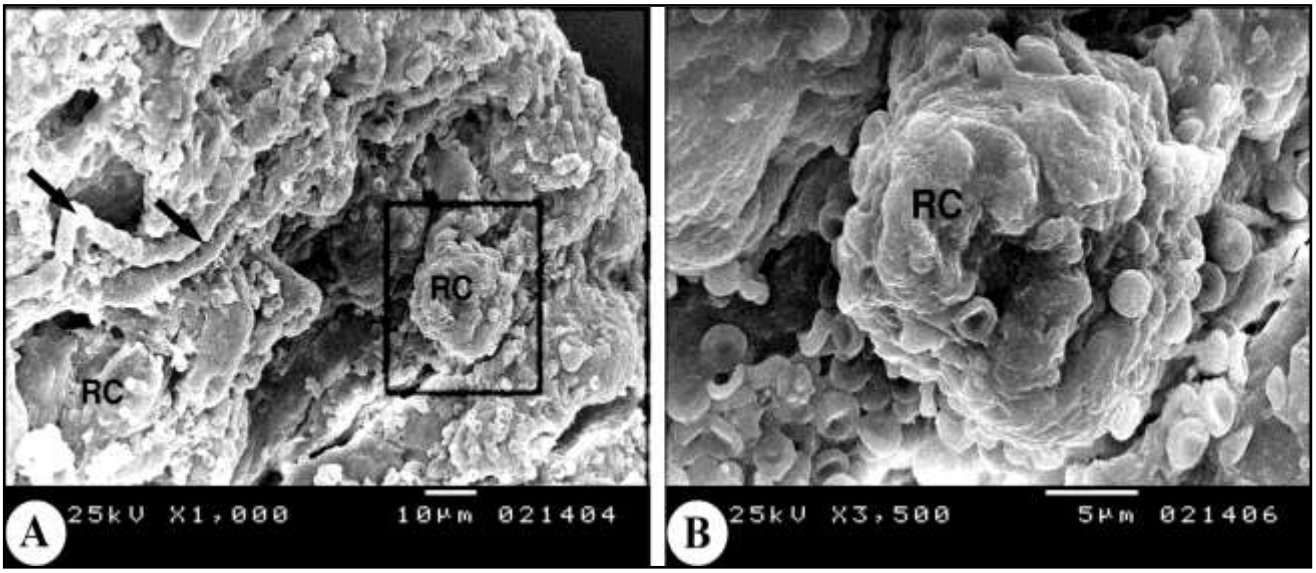


Figure 4. SEM of rabbit kidney at E25 showing the developing renal corpuscles (RC) at low power in A and high power in B, surrounded by renal tubules (arrows).

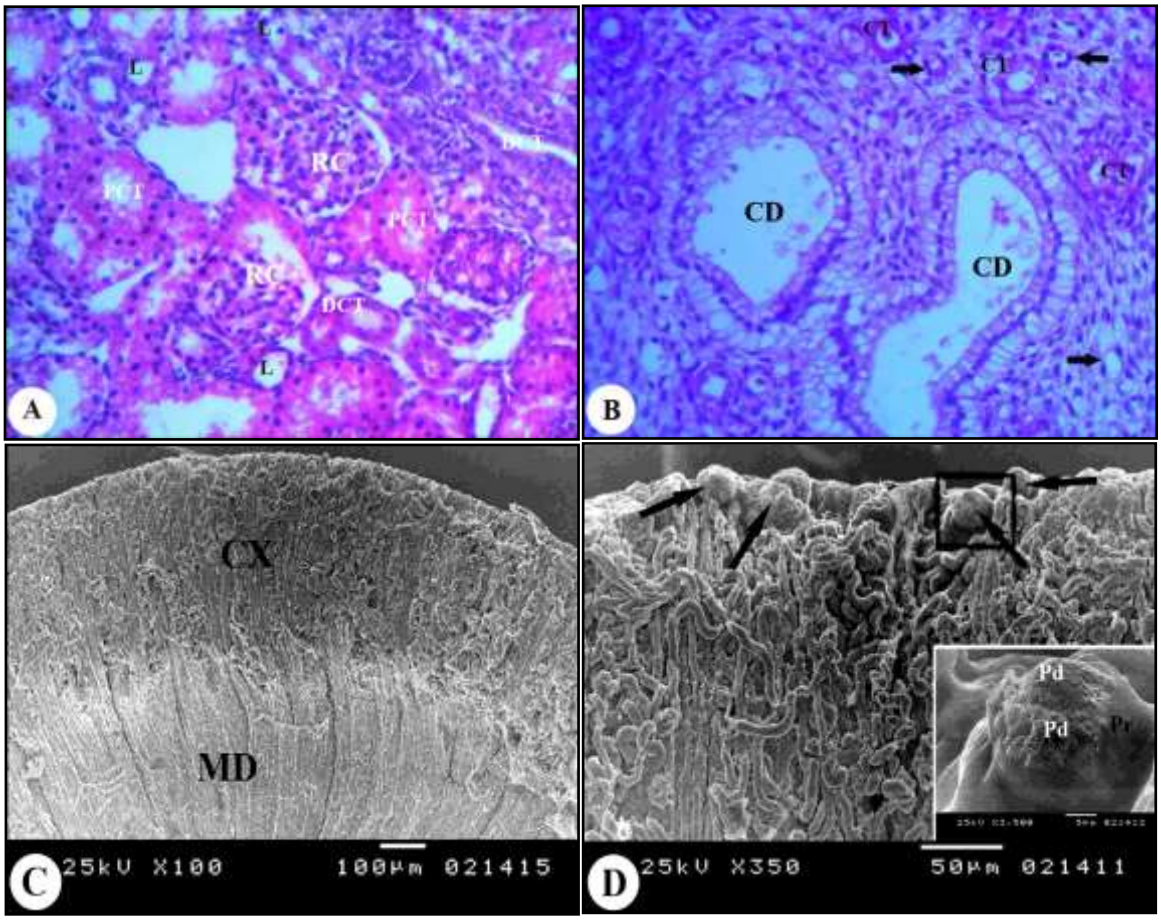


Figure 5. Photomicrograph of rabbit kidney at E30. A; showing the cortex with well developed renal corpuscle (RC), proximal convoluted tubules (PCT) distal convoluted tubule (DCT) and renal loops (L). B; showing the large collecting ducts (CD), collecting tubules (CT), and renal loops (arrows) in the renal medulla. C; SEM showing the differentiation of the cortex (CX) and medulla (MD) in A. B; the renal corpuscles (arrows) surrounded by convoluted and straight segments of renal tubules. The inset showing the renal corpuscle defined in B with its podocytes (Pd) and parietal layer (Pr) of Bowman's capsule. H&E X40 in A and B

At two weeks old, the kidney showed more morphogenesis and the establishment of kidney structure was present. The corpuscles showed clear Bowman's capsules with clear parietal squamous layer. By the end of this period, the characteristic histology of each part of the nephron is developed. The PCT epithelium has well developed brush border, the loops of Henle are identifiable. The medullary rays, collecting ducts and tubules were ascended- obviously- toward the subcortical and cortical zones. In between these ducts and tubules, there were many parallel collagenic fibers (Fig. 7A). The medulla contained collecting duct lined by cuboidal epithelium, the collecting tubules lined by low cuboidal epithelium and renal loops (Fig. 7B). By SEM, podocytes increased in number and their cell bodies and process covered the mature glomerulus (Fig. 7C). The proximal tubules showed narrow lumen and few numbers of cells (Fig. 7D).

At two-months old, the kidney of rabbit with mature histological structure of the renal parenchyma was documented at this stage. The stroma formed mainly of collagen fibers in the capsule in interstitial tissue (Fig. 8A). The typical form of renal corpuscles, formed from Bowman‘s capsule of parietal, visceral layers separated from each other by typical Bowman's space surrounding the glomeruli was noticed. Proximal tubules differentiation is evident by the characteristic deep eosinophilic cytoplasm of their lining cells (Fig. 8B). The medulla became denser and occupied by collecting tubules, ducts and elongating

renal loops (Fig. 8C). PAS stain showed well developed basement membranes of the glomerulus and renal tubules as well as the brush border of PCT (Fig. 8D). By SEM, the mature structure of renal components were noticed where the renal cortex contained renal corpuscles surrounded by the renal tubules (Fig. 8E). The parietal and visceral layers of Bowman's capsule were noticed around the glomerular capillaries. Also the podocytes around the glomerular capillaries were prominent. The renal tubules with different width and diameters filled the spaces between the renal corpuscles. At the vascular pole of renal corpuscles there was DCT with wide lumen as a component of juxtaglomerular apparatus (Fig. 8F).

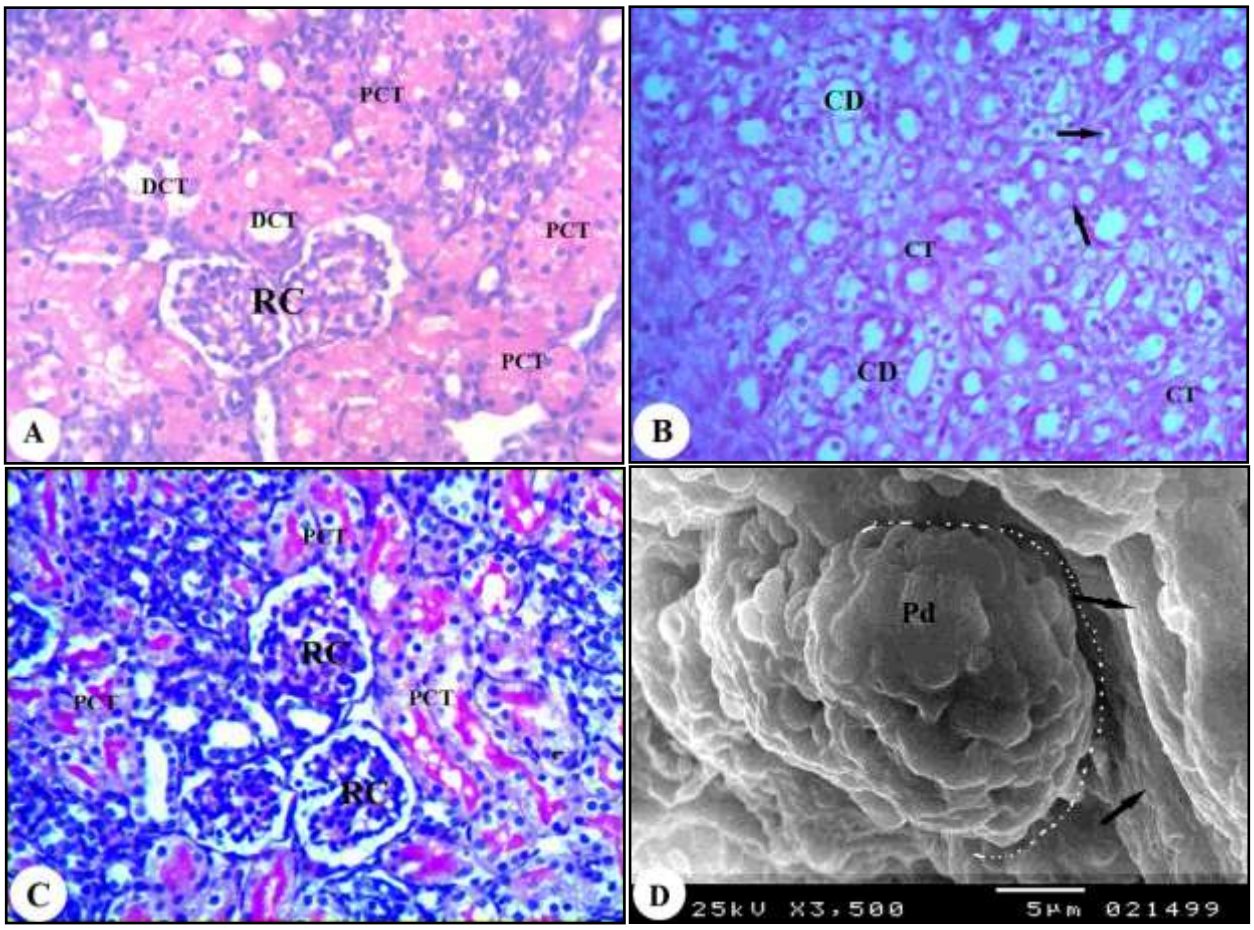


Figure 6. A; Photomicrograph showing the cortex of one week old rabbit with the well developed renal corpuscle (RC), PCT and DCT. B; showing the medulla with the collecting ducts (CD), collecting tubules (CT) and renal loops (arrows). C; showing well developed brush border of PCT. D; SEM showing the renal corpuscle with podocytes (Pd) on the surface of glomerular capillaries and the Bowman's space (dotted line) surrounding them. The parietal layer lined by flattened squamous cells (arrows). H&E in A and B and PAS-alcian blue combination in C X40

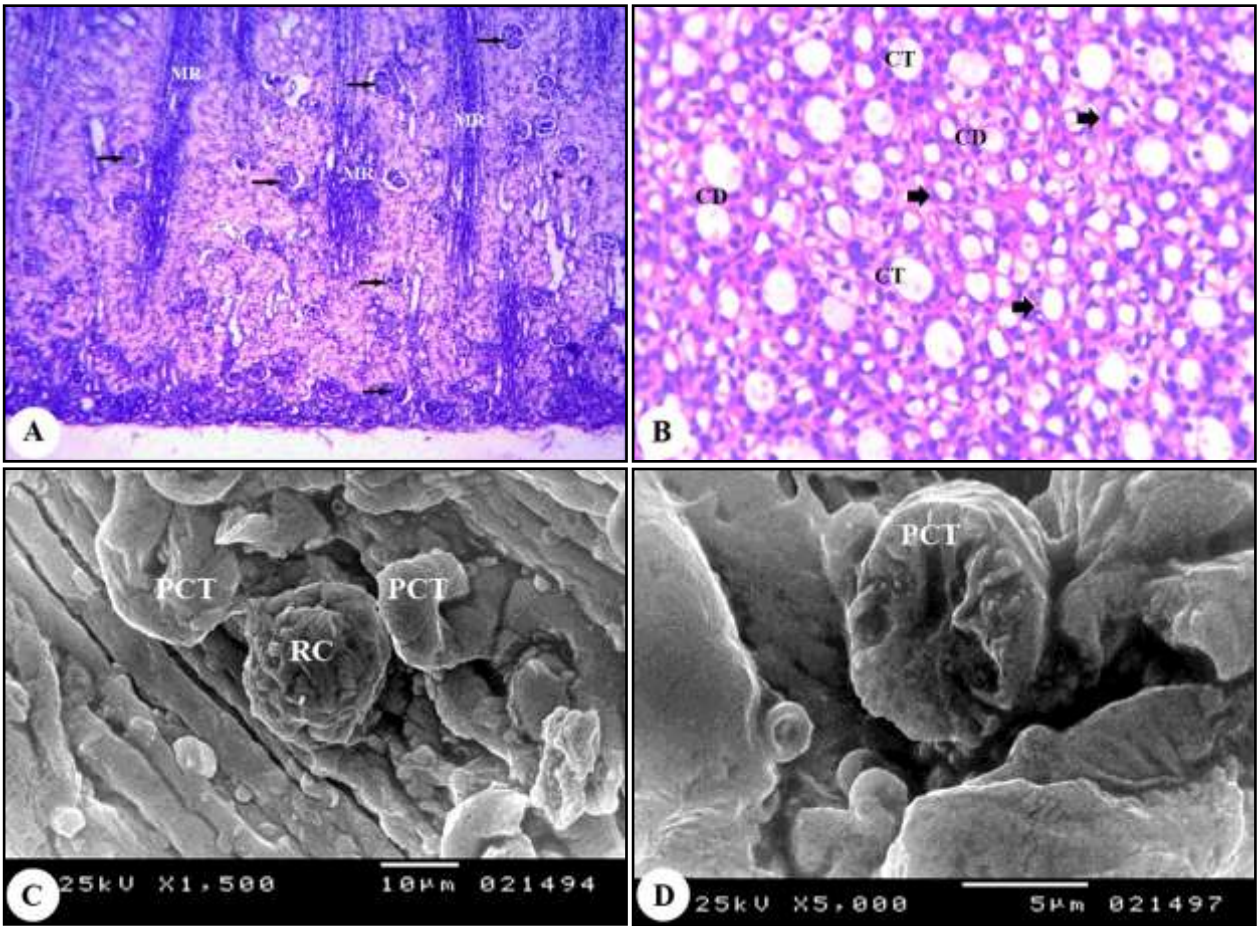


Figure 7. Photomicrograph of rabbit kidney at two weeks old. A; showing the cortex with renal corpuscles (arrows) and medullary rays (MR). B; showing the collecting ducts (CD), collecting tubules (CT) and renal loops (arrows) in the renal medulla. C; SEM showing the renal corpuscle (RC) surrounded by PCT and straight segments of renal tubules. D; SEM of the PCT in cross section with narrow lumen. H&E X40 in A and B

4. DISCUSSION

In the current study we focused and made an intensive investigation to the pre and postnatal development of the kidney of rabbit. This study might be helpful for other fields of research especially experimental teratology and experimental toxicology. At E15 our study showed a large well developed mesonephros and the initial undifferentiated organogenesis of metanephric kidney. Similar developmental view was observed in local Iraqi rabbit's fetuses at 14 days of embryonic life (Jafar and Farhan, 2012). Moreover mesonephros in the rabbit is a large body present in a fully developed state for approximately 4-5 days from 13 to 19 days' gestation (Leeson and Baxter 1957). At this stage, the large mesonephros occupies a great part of abdominal cavity and had a clear position caudodorsal to the liver bud and it cranially situated to metanephros. The same observation was reported by (Latshaw 1987). The large size of mesonephros at this developmental stage is partly responsible for the normal herniation of the growing intestinal loop (Noden and de Lahunta, 1985). While, Sainio (2003), Vetter and Gibley (1966), in mouse, reported that mesonephros situated between somite 10 to 17. In chick, the first mesonephric nephron was seen as depression in the mesonephric blastema on day 3 as reported by Friebova and Goncharevskaya (1982). The result obtained from human showed that the first mesonephric tubules were found at about E25, and they are located at the cranial end of the un-segmented nephric blastema (Marin-Padilla, 1964; Du Bois, 1969; and Tiedemann, 1976). The difference of size and location of mesonephros might be associated with fetus size and the gestation period. Moreover, the size of mesonephros is correlated with the type of placenta (Noden and de Lahunta, 1985). In rabbit mesonephros, there is a tuft of blood capillaries

(glomerulus) penetrates mesonephric tubules to form a double-layered renal capsule, cranial mesonephric duct, lined by high cuboidal epithelium, and caudal mesonephric tubules, lined by low cuboidal epithelium. In contrast Al-Awdan and Kandil (1979), in rat, reported that the mesonephric tubules were lined by double layer of cuboidal epithelium.

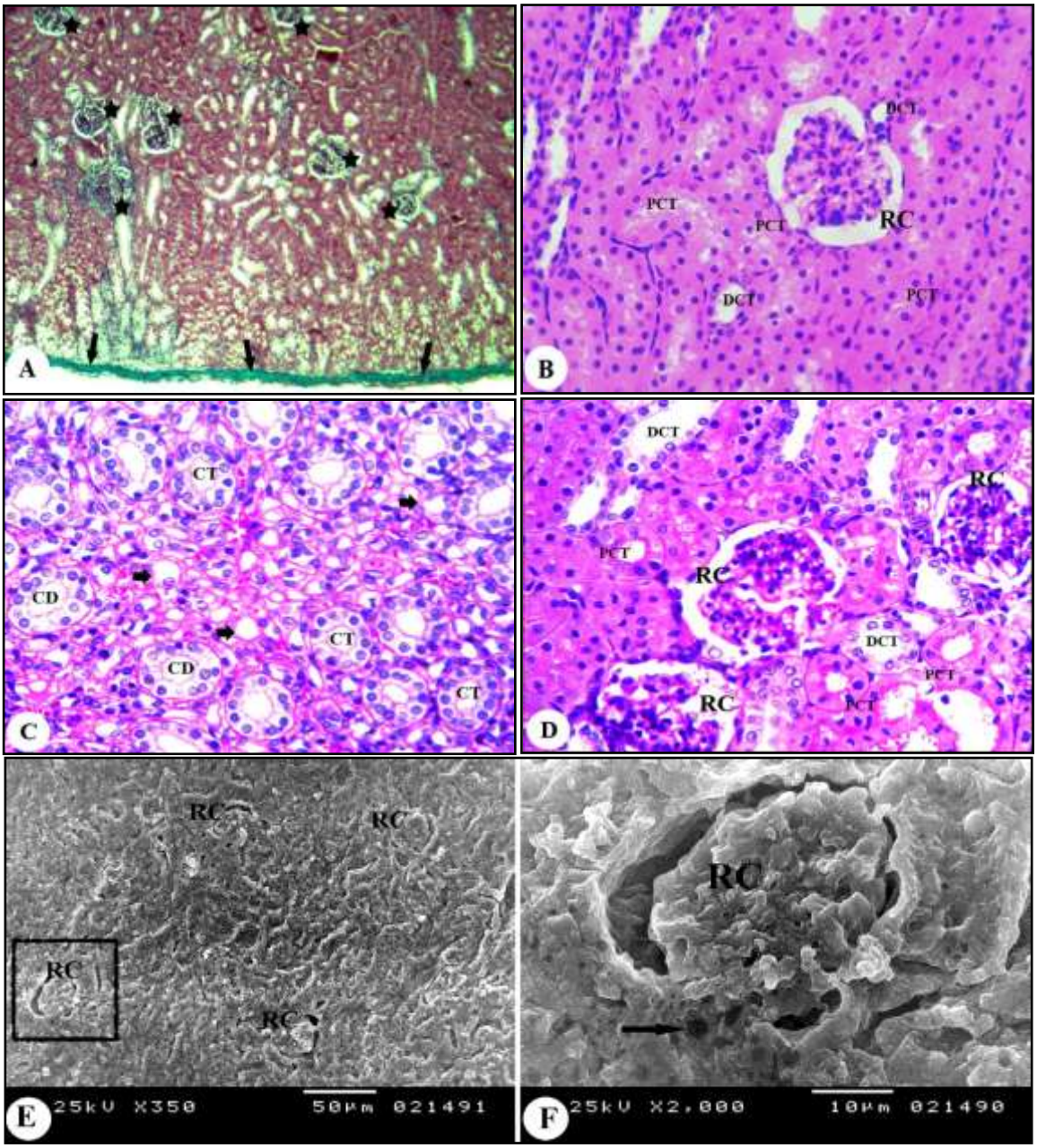


Figure 8. Photomicrograph of adult rabbit kidney (2 months old). A; showing the cortex with mature renal corpuscles (stars) and CT capsule (arrows). B; the renal cortex with mature renal corpuscles (RC), PCT and DCT. C; showing renal medulla in mature form with the collecting duct (CD), tubules (CT) and renal loops (arrows). D; showing well developed tubular basement membranes and brush borders of PCT. E; SEM showing the renal corpuscles (RC) surrounded by renal tubules. F; showing the renal corpuscle (RC), defined in A, with glomerulus surrounded by the Bowman's space and DCT (arrow) near its vascular pole where the JG apparatus is expected. Trichrome stain in A and X4, H&E in B and X40 and PAS in C and D and X40.

The rabbit mesonephric nephron is structurally similar to the adult metanephrogenic nephron; however, the loop of Henle is absent. This result coincides with the results of De Martino and Zamboni, (1966), in human, Tiedemann and Egerer (1984), in pig. In parallel Silverman (1969; cited after Saxen, 1987) stated that there is no direct proof of the functional maturity of the human mesonephric nephrons, and this affirmative view is based on merely structural level.

The rabbit metanephros appears at E15 as an undifferentiated mesenchymal tissue with ureteric bud penetrates it. (Jafar and Farhan, 2012) reported the same observation in local Iraqi rabbit's fetuses at 14 days of embryonic life while (Leeson and Baxter 1957) in 15 days rabbit embryo stated that, the metanephros is present in the pelvis; it is small, immature and not yet at the nephron-forming stage. Evan et al., (1984) documented the appearance of the metanephros at E12.5 in rat, at E11 in mouse, at E23in guinea pig, at E10 in hamster, and at E36 in human while the metanephros of the chick observed at E6. These differences in beginning of tubulogenesis in the metanephros commences may rely also on the length of gestation periods in the different species and the time at which the ureteric bud reach into mesenchyme and divide into multiple branches (Jafar and Farhan, 2012).

At E19, the metanephros kidney of rabbit is located in caudal region of abdominal cavity together with late stages of the degenerated mesonephros. Moderate atrophy was found in the mesonephric tubules and glomeruli, the mesonephric capsules were condensed; the glomeruli were decreased in size. These results are coincided with the observation of (Leeson and Baxter 1957) who reported the same result in rabbit fetuses at the same age. They stated also that, the rostral one-fifth of the mesonephros is degenerate, the glomeruli showing gross thickening of the basement membrane and they are packed with blood cells; the tubules are disrupted and show loss of continuity. Smith and Mackay (1991) and Sainio et al., (1997) found in mouse that the mesonephros began to degenerate at E14.5 and within 24 hours almost all of the mesonephric tubules undergo apoptosis and disappear in a caudal to cranial direction.

On other hands at this developmental stage, the metanephros could be differentiated into inner medulla and outer cortex. In addition, within the cortical region the nephron-forming stage was demarcated where metanephrogenic mesoderm starts to form several solid and canalized renal vesicles. The latter vesicles become elongated tubules and differentiated into the developing nephron and the most advanced one is observed at the corticomedullary junction while the new one appears at the outer part of the cortex. One end of elongated metanephrogenic tubules becomes funnel-shaped that surrounded a tuft of capillaries (glomerulus) forming the renal corpuscle. A similar developmental pattern occurred in mouse where further morphogenesis and differentiation of this S-shaped tubule resulted in the formation of the glomerulus and the distal and proximal tubule elements of the mature nephron (Saxen, 1987). The collecting tubules converge on the papillary duct forming the renal pyramid. This coincides with the described results reported by Cebrian et al., (2004) and Al-yasery (2007) in mice and Mcgeady et al., (2010) in rabbit who claimed that the ureteric bud penetrates the metanephric tissue, which is molded over its distal end as a cap then subsequently the bud dilates, forming the primitive renal pelvis, and splits into cranial and caudal portions, the future major calyces. Each calyx formed two new buds while penetrating the metanephric tissue.

At E25 the newly formed nephrons are concentrated peripherally whereas the early formed nephrons deeply located and showed nearly mature structures. This observation is coincide with the E23 days of rabbit embryos where the metanephros situated now in the upper lumbar region, shows distinct zones of maturity of nephrons, the youngest being cortical. The juxtamedullary ones have an adult morphology and histochemistry (Leeson and Baxter 1957). Hebert et al., (2001) noticed mouse nephrons in superficial or midcortical regions of the kidney with short loops of Henle. More deeply located nephrons (juxtamedullary nephrons) have long loops of Henle. In human, glomerular capillary development began when a single capillary loop grows into the glomerular cleft, which is situated between the primitive podocytes and the proximal tubule of the S-shaped body. As glomerular maturation proceeds, the capillary loop becomes divided into six to eight loops as reported by Potter (1965). The cell bodies of podocytes are setting on the loops of blood capillaries and entirely cover them. A similar finding was reported by Yoshinari and Fujita (1981) in rabbit where the cell bodies of the

podocytes were setting inside the curves of the capillary convolution, but some others were attached to the convex wall of the capillaries.

The medulla at this age points toward the hilum and the pyramid proper and the collecting tubules become relatively visible and well differentiated. At 24 and 26 day rabbit embryo the collecting tubules become visible and show demarcation line between cortex and medulla. Also in this period the first or oldest collecting tubules become enlarged and hereafter taken up into wall of the growing renal pelvis forming undivided kidney with single papilla. Large calyx represented by the entire pelvis and finally visible renal pyramid (Jafar and Farhan, 2012). Fischer et al., (2006), in mice, reported that the elongation of medullary collecting duct is driven by mitosis that aligned with the long axis of the duct. Chaudhury et al., (2006), in goat, mentioned that collecting tubules became visible and differentiated between E56 and E63, while Dickinson et al., (2005) in spiny mouse mentioned that the collecting duct system is visible within the developing medulla at E28. This difference in beginning of tubulogenesis commences relying on the length of gestation periods in each species and the time at which the ureteric bud reaches into mesenchyme and divides.

The collecting ducts characterized by wide lumen and lined by single layer of columnar epithelium where the collecting duct might act as the final regulator of electrolyte balance and water absorption. In an agreement Blomqvist et al., (2004), in mice, the collecting duct consisted, at least, of two functionally distinct cell types arranged in a single layer. They added that these cell types are required for normal acid-base homeostasis and water and electrolyte balance. Moreover Dellmann and Brown (2006) and Bacha and Basha (2000), in domestic animals, mentioned that the epithelial cells of the collecting tubules are pale and vary from cuboidal near the distal tubules to columnar close to the papilla (in papillary ducts).

At E30 the renal corpuscles, with narrow space between the parietal and visceral layers of Bowman's capsule, PCT (with brush border), DCT and loops of Henle are reported here. These results are in agreement with the results of Carrol et al., (2005) in mouse at late stage of gestation. A well developed brush border in the PCT explains its responsibility for reabsorbing the majority of the filtrate. The renal medulla showed longitudinally arranged renal tubules. A similar finding in rabbit was reported in rabbit by Yoshinari and Fujita (1981). Since the primary function of the renal corpuscles is to filtrate the plasma before reaching the proximal tubule so, their development and differentiation occur at this early stage of prenatal life.

Postnatally at age of one-week old rabbit, nephron develops faster with numerous corpuscles at the periphery than at the mid-cortical and subcortical zones and the glomeruli condensate variably from the cortical to the subcortical zones. The glomerulus is the most proximal component of the nephron and the segmentation of the nephron presents a fascinating, but poorly understood process (McCright et al., 2002; Cheng et al., 2003; Leimeister et al., 2003; Cheng and Kopan, 2005). Although we detected well developed renal loops at this age of rabbit kidney Schwartz et al., (1999) reported in mice that the neonatal loops of Henle are relatively short without thin ascending limbs. As maturation occurs, apaptotic deletion of thick ascending cells and transformation into thin ascending limb cells yields a well- defined boundary between inner and outer medulla.

By the end of two weeks old the characteristic histology of each segment of the nephron is distinct and adult form is acquired. The PCT epithelium has well developed brush border, the loops of Henle are identifiable. Nephrogenesis completed 2-3 weeks postnatally in rabbits as found by Seikaly and Arant (1992). Similar results were reported by Neiss (1982) in mouse and Potter (1972) in human. As in mouse, proliferation of the nephron continues, the proximal and distal tubule segments became convoluted while the region between them grows down into the medullary zone to form the loop of Henle. In the rat, nephrogenesis occurred at a rapid rate between birth and 8 days and is completed by 11 days of age (Kavlock and Gray, 1982). Guron et al., (1999), in rat, noticed a continuous tubular differentiation until the time of weaning and functional maturity occurs even later. In mice, nephrogenesis begins on gestation day 11 and is complete by birth (Fouser et al., 1993).

The present study indicated adult kidney of rabbit at age two – months that, the typical form of adult nephron is noticed. The podocytes around the glomerular capillaries were prominent and at the

vascular pole of renal corpuscles there is DCT with wide lumen as a component of juxtaglomerular apparatus. This comes in accordance with the results of Quaggin and Kreidberg (2008) in mouse. This gross structure is important for the functionality of the metanephric kidney as it establishes an osmotic gradient between the cortex and medulla that drives the extraction of water from the urine.

5. Conclusion

The present study was carried out to illustrate the morphogenesis of the kidney of the rabbit with light microscope in addition to the electron microscope during the fetal and postnatal stages of development. The development of the kidney of rabbit embryos and fetuses was concentrated at the early stages. The histogenesis of the mesonephros had been completed early during fetal life while its degeneration, together with the development of metanephros, began at the middle of gestation period and completed by the end of it. The adult form of histological structure of rabbit kidney is reached postnatally by the end of the second week.

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