Histogenesis Of Human Fetal Kidney

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Abstracts: Background: The normal histogenesis of human kidney during fetal life gives us information regarding histological maturation of kidney Objectives: - Present study aims at establishing details of histogenesis of human kidney with time of appearance of various microscopic elements. Methods: - The present study was conducted on kidneys of 59 human foetuses of gestational age ranging from16 to 38 weeks. The pieces of kidneys were processed and paraffin blocks were formed. Sections of kidney were cut which were studied with light microscope after staining. Results: - The subcapsular nephrogenic zone became narrow with increasing fetal age and disappeared at 38 weeks of gestation. In cortex, differentiation occurs from centre to periphery as indicated by more number of mature renal corpuscles and well differentiated proximal convoluted tubule, distal convoluted tubules in deeper part than superficial part of cortex. As the fetal age increases, the number of well differentiated tubules seen in medulla went on increasing. The histological structure of kidney was almost similar to kidney at 35 weeks of gestation. Conclusion:-This may help us in understanding various renal disorders. This study can also be used for determination of age of fetus. [Patil S et al NJIRM 2012; 3(3) : 122-127]

Key words: Gestational age, Human fetal kidney, Medulla, Renal cortex.

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Introduction: Introduction: The development of human organs is an ongoing process which begins with fertilization and continues in postnatal life. It is well known fact that function of an organ depends on histological maturation of an organ. The development of human kidney exhibits unique feature where three slightly overlapping renal systems i.e. the pronephros, mesonephros and metanephros are formed. The first two disappear and the last one develops into permanent kidney. The permanent kidneys become functional in intrauterine life and urine produced by them is added to amniotic fluid from 10th week of gestation[1].

Since the beginning of 19th century work has been done on structural development of kidney. Bowman [2] thought that during development of renal corpuscle, the Bowman's capsule was perforated by afferent and efferent vessels. Gerlach[3] stated that when capillaries penetrated the capsule, they must push capsular cells ahead of them instead of breaking through as Bowman has assumed. Toldt[4] described hollow S- shaped structure arising from metanephric blastema; the upper two limbs of which became convoluted tubules and Henle's loop while the lower limb became Malphigian corpuscle. According to Netter[4] , in the 10th fetal month , the nephrogenic tissue disappeared, suggesting that there was no postnatal nephron development. According to Helena Maria et al[5] nephrogenesis in human started at 6th week of intrauterine life and completed by 35th week of gestation. After 25 weeks the glomeruli formed the cortical layer making corticomedullary differentiation more distinct. The tubules in differentiation were numerous between 25 to 30 weeks period .

The description of development of human kidney given in various textbooks of embryology[6,7,8,9] 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: After taking permission from human ethical committee the present study was conducted on kidneys of 59 human fetuses of gestational age ranging from 16 weeks to 38 weeks. The fetuses were obtained from department of obstetrics and gynaecology, Sassoon General Hospitals, Pune after taking written consent from parents. These fetuses included medically terminated, spontaneously aborted and the still

born. Twins and fetuses with gross anomalies were omitted from the study.

Gestational age of each fetus was calculated from crown-rump lengths[10]. The fetuses were dissected by taking midline incision on anterior abdominal wall and both kidneys were taken out. The kidneys were kept in 10% formalin for 2-4 days. The pieces of kidney having thickness less than 0.5 cm were cut. These were processed and paraffin blocks were prepared. Sections having 5-10 microns thickness were cut using rotary microtome. Sections were then stained with haematoxylin and eosin. The microscopic appearance of developing fetal kidney was studied at various ages using light microscope.

Result: Histology of kidney was studied by examining slides after staining with haematoxylin-eosin. Histological structure was as follows:

A.15-18 weeks of gestation: 16 weeks stage of kidney:- Nephrogenic zone was seen just beneath the capsule (photomicrograph 1). This nephrogenic zone consisted of closely placed spindle shaped cells having faint eosinophilic cytoplasm and oval dark staining nuclei. Deep to nephrogenic zone some S- shaped tubular structures were seen lined by columnar cells with eosinophilic cytoplasm and dark stained oval nuclei (Photomicrograph 2). Deep to nephrogenic zone developing renal corpuscles were seen dispersed in parenchyma which showed different developmental stages as shown in photomicrograph 2.

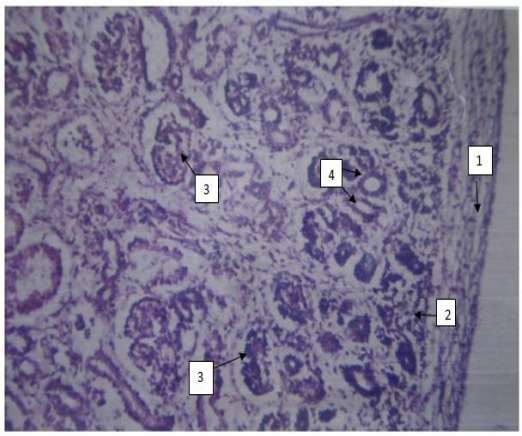
Stage I: - Bowman's space was crescentic enclosing few capillaries. The visceral and parietal layers of Bowman's capsule were lined by simple columnar and low cuboidal epithelium respectively.

Stage II: - Glomerulus consisting of capillaries was almost completely surrounded by Bowman's space. The visceral layer of Bowman's capsule was still lined by simple columnar cells but the parietal layer was lined by low cuboidal to flat cells. The base of glomerulus was broad.

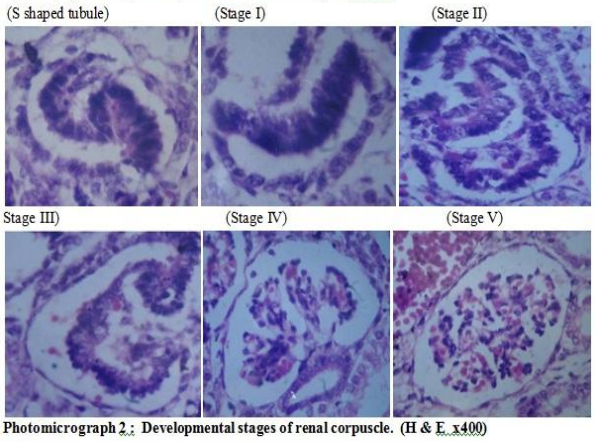
Stage III: - The proliferating capillaries invaginated the concave visceral wall of Bowman's capsule showing beginning of lobulations in glomerular tuft. The visceral epithelium was still continuous and simple columnar while the parietal epithelium was simple squamous.

Stage IV: - Well marked lobulations were seen in glomerulus. Visceral layer was now formed by cuboidal cells and it was discontinuous. Parietal layer was formed by simple squamous epithelium.

Stage V: - Mature renal corpuscle showing network of glomerular capillaries. Visceral layer was represented by few cells scattered singly over the surface of glomerular tuft. Parietal layer was formed by squamous cells. The Bowman's Space was seen between two layers.



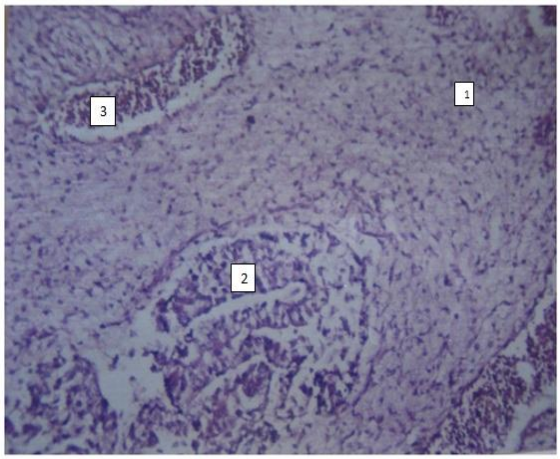
Photomicrograph 1: Cortex of 16 weeks kidney showing 1)capsule 2)nephrogenic zone 3)developing renal corpuscle 4)undifferentiated tubules. (H & E, x100)



Photomicrograph 2 : Developmental stages of renal corpuscle. (H & E, x400)

As we went deeper from the capsule, the more developed stages of renal corpuscles were seen with rudimentary renal corpuscles in superficial part and mature renal corpuscles in deeper part. The tubules in cortex were lined by single layer of cuboidal cells with pale eosinophillic cytoplasm and vesicular nuclei. These tubules could not be differentiated into proximal or distal convoluted tubules (Photomicrograph 1). In between tubules

and glomeruli, the connective tissue was seen. In medulla, along with connective tissue and primitive blood vessels few clusters of cells were seen indicating beginning of formation of irregular tubular structures (Photomicrograph 3).



Photomicrograph 3: Medulla of 16 weeks kidney showing 1)loosely arranged mesenchymal cells 2)clustering of cells 3)blood vessels containing RBCs. (H & E x100)

18 weeks stage of kidney:- Histological features were more or less similar to that of 16 weeks stage with following modifications

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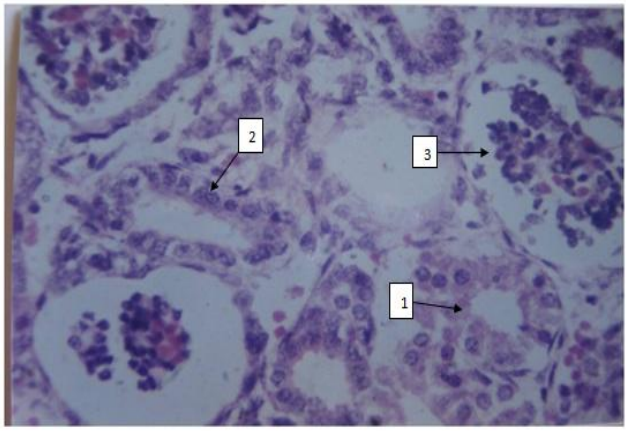
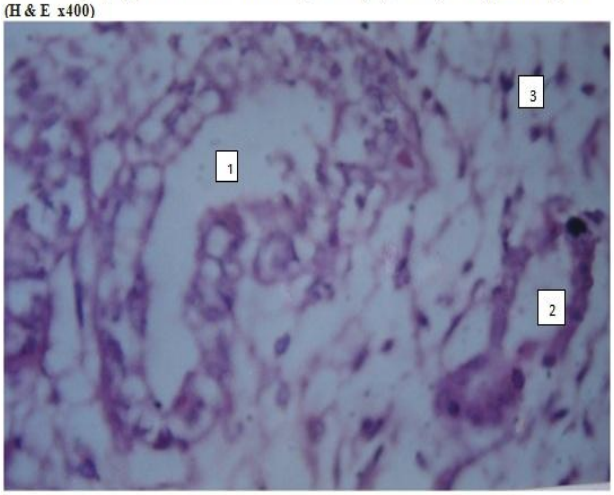
Cortex: - More number of renal corpuscles and tubules were seen while connective tissue amount was reduced. Most of the tubules in cortex were still in undifferentiated form but few tubules could be identified as proximal convoluted tubule (PCT) or distal convoluted tubule (DCT). PCT showed small irregular lumen and were lined by large pyramidal cells with intense eosinophilic cytoplasm with brush border at places and round euchromatic nuclei. DCT had wide regular lumen and were lined by cuboidal cells with pale eosiniphillic cytoplasm and round euchromatic nuclei (Photomicrograph 4).

Medulla:-Few irregular tubular structures were seen. Some of these tubules could be identified as collecting tubules and thick segments of loop of Henle. Collecting tubules were lined by simple columnar epithelium with clear cytoplasm, distinct cell margins and vesicular nuclei. The thick segment of loop of Henle was lined by simple cuboidal epithelium with eosinophillic cytoplasm and euchromatic nuclei (Photomicrograph 5)



Photomicrograph 4 : Cortex of 18 weeks kidney showing 1)PCT 2)DCT 3)renal corpuscle (H & E x400)

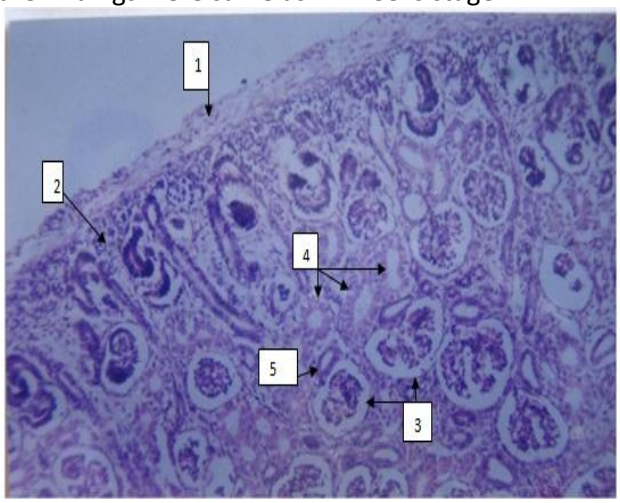


Photomicrograph 5 : Medulla of 18 weeks kidney showing 1)collecting tubule 2)thick segment of Henle,s loop 3)loosely arranged mesenchymal cells. (H & E x400)

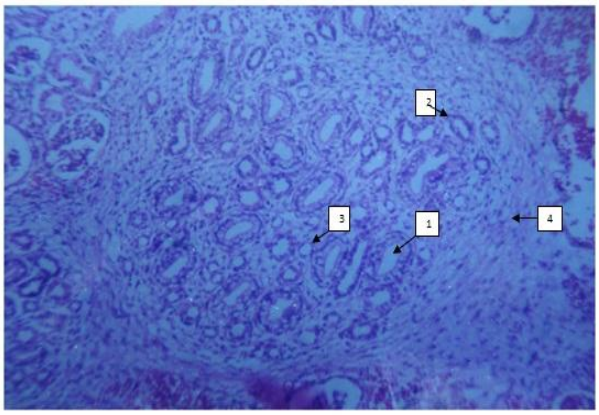
B. 19- 26 weeks of gestation:

As gestational age increased from 19 weeks to 26weeks, the cortex showed more number of renal corpuscles and tubules and less amount of connective tissue. The developing renal corpuscles were still dispersed in parenchyma till 23 weeks .From 23 weeks onwards corticomedullary differentiation became more distinct. More number of PCT and DCT could be indentified in deeper part of cortex. PCT were more in number than DCT. With increasing gestational age from 19 weeks to 26 weeks medulla showed increase in the vascularity and number of tubules while there was decrease in connective tissue. The collecting tubule and thick loop of Henle were seen distinctly. From 20 weeks onwards tubules were seen which were lined by simple squamous epithelium and had small lumen. These were thin segments of loop of Henle. (Photomicrograph 6, 7, 8)

C. 27-30 weeks of gestation: At 27 weeks, the structure of kidney was almost same as 26 weeks stage but cortex and medulla both showed increased thickness. The medulla showed more number of blood capillaries. At 29 weeks, the thickness of subcapsular nephrogenic zone was reduced and it formed a thin layer. The cortex increased in thickness and the medulla showed more number of collecting tubules and also the thick and thin segments of loop of Henle. Rest of the findings were same as 27 weeks stage.

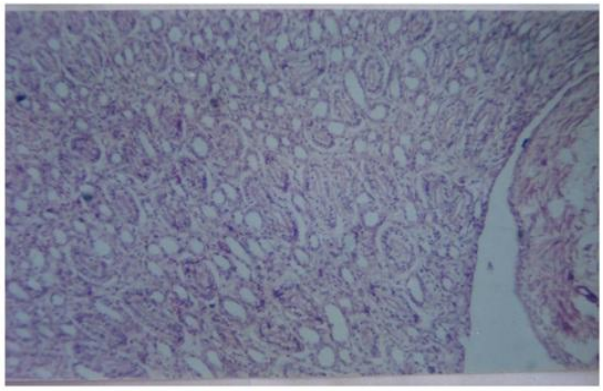


Photomicrograph 6 : Cortex of 20 weeks kidney showing 1) capsule 2)nephrogenic zone 3)developing renal corpuscle 4)PCT 5)DCT. (H & E x100)

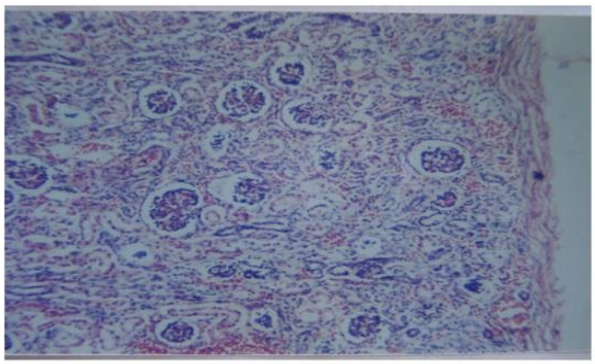


Photomicrograph 7 : Medulla of 20 weeks kidney showing 1)collecting tubule 2)thick segment of Henle,s loop 3) thin segment of Henle,s loop 4)loosely arranged mesenchymal cells. (H & E x100)

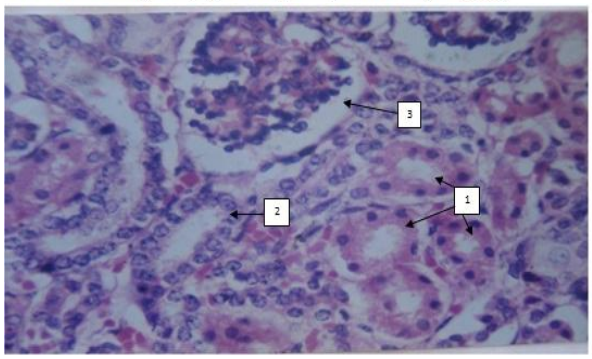
D. 31-38 weeks of gestation: At 31 weeks, the subcapsular nephrogenic zone was thin and interrupted at places (photomicrograph 9). In cortex, the first stage of developing renal corpuscle was not seen. The superficial renal corpuscles were also well differentiated and showed advanced stages of renal corpuscle development. In medulla, most of the collecting tubules were now lined by single layer of cuboidal cells. At 35 weeks, the subcapsular nephrogenic zone was narrow and interrupted at many places by developing tubules and renal corpuscles. The cortex showed more number of mature stage V renal corpuscles. The cortex and medulla showed increase in thickness and vascularity (photomicrograph 10, 11). At 38 weeks the subcapsular nephrogenic zone disappeared. The cortex showed absence of undifferentiated tubules. Rest of the findings was same as 35 weeks stage.



Photomicrograph 8 : Medulla of 26 weeks kidney showing whole of the medulla packed with developing tubules & reduced connective tissue. (H & E x100)



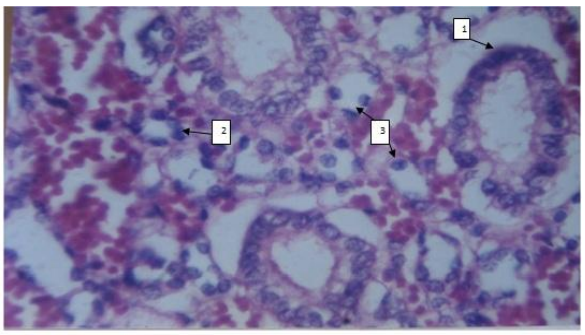
Photomicrograph 9 : Cortex of 31 weeks kidney showing discontinuous nephrogenic zone and rest of the field showing developing renal corpuscles, PCT & DCT. (H & E x100)



Photomicrograph 10 : Cortex of 35 weeks kidney showing almost adult structure with 1)PCT 2)DCT 3)renal corpuscle (H & E x400)

Discussion: The permanent kidney develops from three sources[6] – a) metanephric blastema which provides excretory units, b)the ureteric bud which gives rise to collecting system and c)angiogenic

mesenchyme which migrates into metanephric blastema to produce glomeruli and vasa recta. The standard textbooks do not describe much details of histogenesis of kidney [1,6,7,8,9]. In present study the histological structure of kidney was studied at various gestational ages. The findings of present study were compared with that described by different scientists.



Photomicrograph 11 : Medulla of 35 weeks kidney showing almost adult structure with 1)collecting tubule 2)thick segment of Henle,s loop 3)thin segment of Henle,s loop . (H & E x400)

I)Nephrogenic zone :- Formation of nephron begins approximately during the 8th week of intrauterine life in humans[11]. According to Helena et al[5] nephrogenesis begins at 6th week and continue till 35th week of gestation. After 35th week maturation of nephron continues but neoformation of nephrons do not occur as indicated by disappearance of nephrogenic zone after 35th weeks of gestation. Aschoff[12] found the persistence of nephrogenic zone upto 3-6 months after birth suggesting that new nephron formation continues postnatally. In present study nephrogenic zone was seen just beneath the capsule as a broad and continuous zone in earlier weeks of gestation but as fetal age increased the size of nephrogenic zone decreased and it was absent at 38 weeks of gestation indicating that after 38 weeks of gestation new nephrons were not formed. These findings of our study are in agreement with the findings of Morag et. Al.[13]

II) Cortex of kidney: - All stages of nephron differentiation are present concurrently in the developing metanephric kidney[6]. In present study also almost all stages of developing renal corpuscles (Stage I to V) were seen in each specimen studied. Immature renal corpuscles were seen in superficial part and more mature renal corpuscles were seen in deeper part of cortex. Rudimentary renal corpuscles (stage I) were seen in more number in early part of gestational period and they were absent after 31st week of gestation. Helena Maria et al [5] had found rudimentary renal corpuscles till 35 weeks whereas Arne Ljungqvist[14] found rudimentary renal corpuscles even at full term. According to Moore [8] the number of glomeruli increased from 10th to 32nd week gestation when an upper limit is reached. In our study the number of mature renal corpuscles went on increasing with increasing gestational age being abundant after 35 weeks.

At 18 weeks of gestation proximal and distal convoluted tubules were seen in cortex for the first time in our study. With increasing gestational age, the number of well differentiated proximal and distal convoluted tubules went on increasing. Mature tubule appears first in inner cortical area[7].

In our study more number of mature renal corpuscles and tubules were seen in deeper part than in superficial part of cortex. These findings suggest that cortex of kidney differentiates from deeper to superficial part. Helena Maria et al[5] also had similar findings.

III) Medulla: - In present study the medulla showed connective tissue, primitive blood vessels and few clusters of cells at 16 weeks of gestation. At 18 weeks, few collecting tubules and thick ascending loop of Henle were seen. At 20 weeks in addition to these tubules few thin segment of Henle's loop were also seen. Presence of Henle's loop in metanephric kidney is responsible for production hypertonic urine.[6] The findings of Arne Ljungqvist[14] agree with our observation that as gestational age increased the number of well differentiated tubules in medulla increased. But Arne Ljungqvist had not mentioned regarding the time when collecting tubules and Henle's loop appeared in medulla. Many of the earlier studies did not elaborate much regarding development of renal medulla.

According to our study thickness of cortex and medulla increased gradually throughout the gestational period studied. Tsuda[15] had similar findings. Helena Maria et.al[5] states that the renal corpuscles were dispersed in parenchyma of kidney till 25th week of gestation after which they formed a cortical layer making the corticomedullary

differentiation more distinct. Our findings agree with this observation.

Conclusion: Nowadays the premature babies can be made to survive successfully because of advances in medical field. For this purpose the information regarding the functional status and histological maturation of different vital organs becomes significant. In this regard our study gives information about histological development of human kidney and the time sequence in which it develops. This study can also be used for determination of age of fetus for medico-legal purpose.

References:

1. William J. Larsen. Development of urogenital system. Human Embryology 3rd Ed. Churchill Livingstone Publishers Philladelphia 2001; 273.
2. Bowman W. Structure and use of Malpighian bodies of kidney with observations on circulation through that gland.Philos, Tran: (A/B) London 1842; 132:57.
3. Gerlach J. Contributions to the theory of structure of the kidney. Archives of Anatomy Physiology and scientific medicine. 1845; 363-386.
4. Potter L. Development of the human glomerulus. Archieves of pathology 1965; 80:241-255.
5. Helena Maria, Lizardo-Daudt et al. Diagnosis of the human age based on the development of normal kidney. Journal Brasileiro de patologia e medicina Laboratorial 2002; 38(2):1-10
6. Peter L. William Development of urinary system. Gray's Anatomy .38th ed. Edinburgh Churchill Livingstone Harcourt Publishers Limited 2002; 199-204.
7. Hamilton W.J. Boyd and Mossman.Histogenesis of metanephrons. Human Embryology. 4th ed. The University of Michigan Heffer Publication 1972: 383-391.
8. Keith L. Moore and T.V.N. Persaud. Development of urinary system. The developing Human. 7th ed. The University of Michigan Saunders publisher 2003; 288-292
9. Sadler T.W. Urogenital system Langman's medical embryology 9th Ed. Lippincott Williams and Wilkins Baltimore 2006;229-238
10. Hamilton W.J. Boyd and Mossman.Growth of embryo and fetus, development of external form,estimation of embryonic and fetal ages. Human Embrology 4th ed. The University of Michigan Heffer Publication 1972; 175.
11. Clapp, W. L. and Tisher,C.C. Gross anatomy and development of the kidney. Renal Pathology with clinical and functional correlations Philladelphia; Lippincott 1989;67-89.
12. Campos E.S. Pathological changes in kidney in congenital syphilis John.Hopk.Hosp.Bull 1923; 34: 253-262.
13. Morag S. Mac Donald and John L. Emery. The late intrauterine and postnatal development of human renal glomeruli. Journal of Anatomy 1959; 93:331-340
14. Arne Ljungqvist. Fetal and post natal development of intrarenal arterial pattern in man: A microangiographic and histologic study. Acta Paediatrica 1963; 52: 443-464.
15. Tsuda. Histologic investigation of fetal kidney. Jap. J. Obstet. Gynec 1943;17:227-341