DEVELOPMENT OF HUMAN KIDNEY---- A STUDY OF EARLY FOETAL STAGES

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ABSTRACT

The present study has been under taken to review the prenatal development of kidney in human fetuses of Indian origin. With the advent of modern technology & equipments for diagnostic and therapeutic procedures in the field of medical science, it becomes imperative to have sound knowledge of basic human morphology & developmental anatomy. The present work is an attempt to analyse the growth pattern of kidney in human fetuses, which may prove useful in defining the foetal kidney diseases such as agenesis, hypolpasia, multicystic kidney, polycystic kidney etc., In this process, foetuses of 1st, 2nd & 3rd trimesters obtained from local hospitals have been subjected to protocol of dissection, processing & staining procedures already in existence.

Key words: metanephric blastema, ureteric bud & glomeruli

INTRODUCTION

The development of many organs starts with folding and multiplication of an epithelial sheet that progresses into the formation of a bud. Elongation of the bud forces the rudiment of this proto-organ to invade surrounding tissue, frequently composed of mesenchyme, known as metanephric blastema. The angiogenic mesenchyme migrates into metanephric blastema to form glomeruli & vasa recta[1,2,3,4,5,6]. Kidney size is presumably influenced both by genetic and environmental factors. The number of glomeruli at birth is presumably genetically determined. The size of kidneys is dependent on the number and size of nephrons [6,8]. According to Behrman & Almeida the retardation of renal development, as occurs in individuals of low birth weight, gives rise to increased postnatal risk of systemic and glomerular hypertension, as well as enhanced risk of expression of renal diseases such as aplasia, hypoplasia, cystic disease or renal agenesis.

In view of the dynamic changes in the mesenchymal cells of intermediate plate of mesoderm, preliminary observations are being taken up as a subject to study histogenesis of kidney in the fetuses & also the available literature is mostly on the works in other countries.

MATERIALS & METHODS

50 still born foetuses of different gestational age groups ranging from 10 weeks to 40 weeks (table 1) were collected from local nursing homes of vizianagaram. Foetuses were dissected & kidneys were removed & fixed in 10% formalin. The morphometric data i.e., length & width were taken by slide calipers. (table 2) The weights of both kidneys were taken & the volume of each kidney was measured by Archimides principle (water displacement method)(table3). The coronal sections of kidneys were subjected to routine histological preparation. The H&E stained slides were studied under light microscopy.

OBSERVATIONS

Macroscopic appearence:

The metanephric kidney appears oval with a smooth surface having no lobular pattern at 10 weeks. Lobulations were identified at 14wks gestation & fusion of the lobules was noted between 16-20wks gestation (fig 1). No lobulation could be visualized beyond 24 wks gestation. Reniform appearance attained at 32wks gestation.

Morphometric data:

The mean length of right (RT) kidney ranged from 0.44cm (10wks G.A) to 4.2cm (40wks G.A), whereas the left (LT) kidney measured from 0.45cm (10wks G.A) to 4cm (40wks G.A) (table 2)

The mean width at the hilum of Rt kidney ranged from 0.18cm (10wks G.A) to 2.1cm (40wks G.A), whereas the Lt kidney varied from0.16cm (10wks G.A) to 2cm(40wks G.A) (table 2)

The mean weight of Rt kidney ranged from 200.8mg (10wks G.A) to 5600mg (40wks G.A), whereas the Lt kidney measured from 200mg (10wks G.A) to 5500mg

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(40wks G.A)(table 3). A steep increase in weight of kidneys was noted at 22nd wk.

The mean volume of Rt kidney ranged from 0.25ml (10wks G.A) to 6.2ml (40 wks G.A), whereas the Lt kidney varied from 0.24ml (10wks G.A) to 6ml (40wks G.A)(table3). A gradual increase in the volume of kidney was noted.

Microscopic observations:

10weeks:

Surface of kidney was smooth without any clefts, indicating lobulation has not yet been started (fig2a). Ampulla formation from branched ureteric bud was noted. The Undifferentiated mesenchymal cells were evenly distributed throughout the section & at places they clustered together (fig2b).

12 weeks:

The periphery of the section showed indentations & lobulations (fig3a), the lobulated masses being occupied by still undifferentiated mesenchymal cells and glomerular formation having been started. Metanephric cells showed dark stained nucleus & cavitation among the clustered cells appeared at the central zone. Most of the developing tubules were in the vesicle stage (Fig 3b).

14 weeks:

Lobular pattern was still predominant with deep clefts in between lobes being identified (fig 4a). There was a thick capsule around the parenchyma & septae protruded from the thick capsule. The 'C'& 'S' shaped developing glomeruli were seen. Juxta glomerular apparatus could be identified near few glomeruli. (Fig4b) Sections of renal tubule appeared in the medullary region. (Fig4c). Formation of collecting tubules with their characteristic lining of cuboidal epithelium with prominent nuclei occupying deeper part of the kidney were observed. However plenty of undifferentiated mesenchymal cells were still seen occupying the areas in between the glomeruli in the cortex & collecting tubules in the medullary region.

16 weeks to 18 weeks:

Definite capsule with few &small septae were noticed. (Fig 5) No evidence of lobulation was appreciated by the presence of continuous cortex. The peripheral area was deeply stained indicating increased activity while medulla showed mesenchymatous tissue with some developing tubules. Proximal Convoluted Tubule (PCT) Distal Convoluted Tubule (DCT) with their characteristic cuboidal epithelium were noted. Transition zone appeared between cortex and medulla. Papilla of pyramid was clearly seen indicating tertiary division of renal pelvis i.e., minor calyx. (Fig5) Deeper glomeruli were larger.

20 weeks to 22 weeks:

Periphery of the kidney still showed clefts, indicating the lobular pattern of earlier weeks (fig 6). Cortex appeared as uniform zone. Cortico medullary junction was well defined. Juxta glomerular apparatus was well defined with the evidence of existence of mesangial cells. Juxta medullary glomeruli were very large. (fig 6)

24 weeks:

Clear demarcation of cortex & medulla along with well defined juxta medullary glomeruli arranged in multiple rows were noted. Both limbs of loops of henle & the collecting ducts were noted. Arrangement of sectioned parts of renal tubule indicated increase in their length. Renal pyramid formation was complete with prominent papillae. (fig 7)

25 weeks to 40 weeks:

Surface is smooth without any lobulation. Evidence of mesenchymatous tissue at the periphery i.e., Nephrogenic zone was still present, but the thickness decreased with increase in the gestational age. Cortex & medulla were further differentiated (fig 8a&8b). Well defined pyramidal system was delineated.

EMBRYOLOGY:

The kidney is developed from metanephric blastema& ureteric bud. Secretory part appears as small filtering units, nephrons. Cranial nephrons function for a short period and were named as pronephros. The nephrons formed at the thoraco lumbar level & grouped as Mesonephros, which develop connection with each other to form a longitudinal channel-mesonephric duct. Those nephrons, which formed at the sacral level of intermediate mesoderm of embryo, group together to form Metanephros. A diverticulum appears on mesonephric duct, which have an affinity to grow towards metanephros. The branches of ureteric bud

develops communication with all the nephrons. Thus secretory part of nephron is formed by metanephros & collecting part is formed by ureteric bud. The angiogenic mesenchyme migrates into metanephric blastema to form glomeruli & vasa recta[1,2,3,4,5,6]. The process of renal development begins at deeper regions and reaches the peripheral part of the cortex with the advancement of ampulla in that region and terminates during the The process of renal development begins at deeper regions and reaches the peripheral part of the cortex with the advancement of ampulla in that region and terminates during the last month of gestation with subsequent interstitial growth.[7,5,6]

DISCUSSION

The morphological study outlines the presence of lobulation at 12wks, while at 16wks the lobulation is not evident in sections, which is in agreement with previous authors[5,6]. In the present study the development of tubules from vesicle to 'S' shaped body as described by various authors[7,4,10,11] (fig 9). Development of well defined arcade system during 18wks is in accordance with previous authors[5,6]. An important observation that stood significantly is the appearance of juxta glomerular apparatus at 14 weeks gestation (fig 4b) & difference in staining pattern of tubules at 16 weeks of gestation, which found no mention in the literature of earlier authors. Two types of tubules, one being deeply basophilic & the other being eosinophilic with large lumen and rounded nucleus (fig 10). The current study reveals that major development of kidney takes place around 20th to 22nd week of gestation as evidenced by the increase in weight and the morphometric parameters of the kidney. The present study illustrates a sequential view of human renal development in light microscopy, as disorganized mesenchymal cells become highly organized epithelial tubules, which will be useful for identifying renal anomalies by utilizing available modern imaging techniques. The present study also can give an indication to the obstetricians and neonatologists for taking more care and making the pregnant mothers aware of the changes that are likely to takes place from mid-gestation to till the last week of gestation

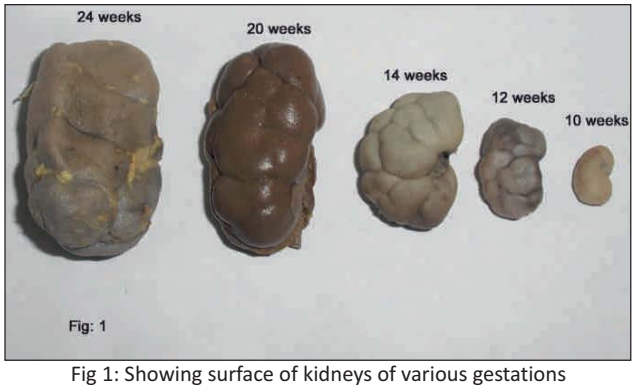

Fig 1: Showing surface of kidneys of various gestations

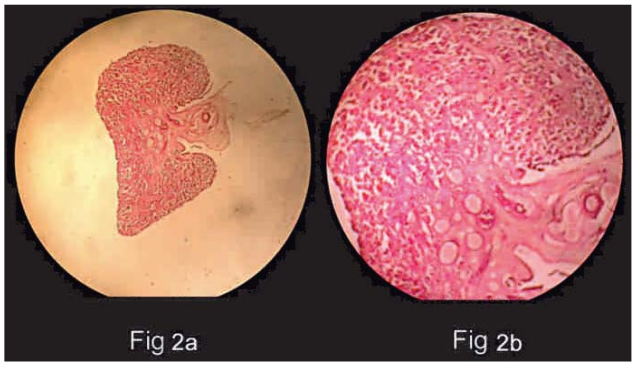

Fig 2a: Showing the panoramic view of L.S of Kidney at 10 wks G.A, 10x4
Fig 2b: Showing clusters of undifferentiated mesenchyme, L.S of Kidney at 10wks G.A, 10x10

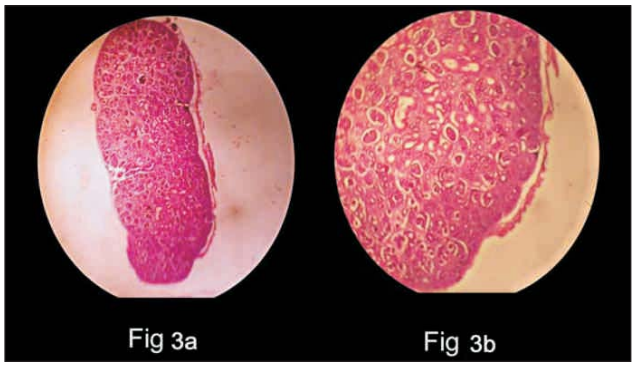

Fig 3a: Showing panoramic view of L.S of Kidney at 12 wks G.A, 10x4
Fig 3b: Showing developing tubules in differentiated lobules, 12 wks G.A, 10X10.

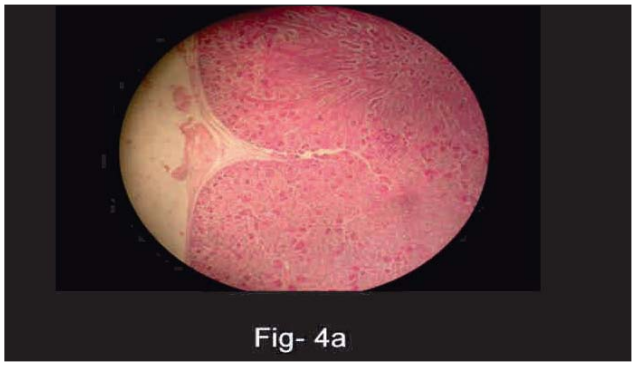

Fig 4a: Showing deep clefts in L.S of Kidney, 14 wks G.A, H&E, 10X10.

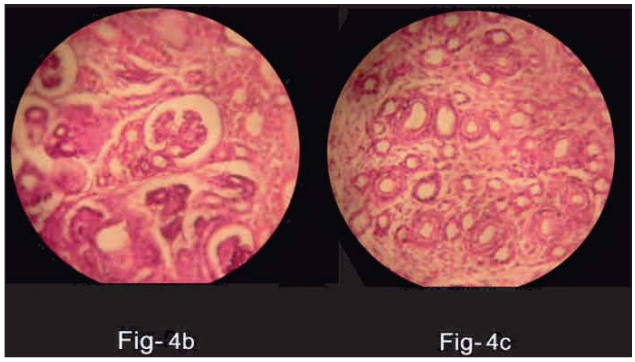

Fig 4b: Showing juxta glomerular apparatus, 14 wks G.A, H&E, 10X40.
Fig 4c: Showing sections of tubules in medulla, 14 wks G.A, H&E, 10X40.

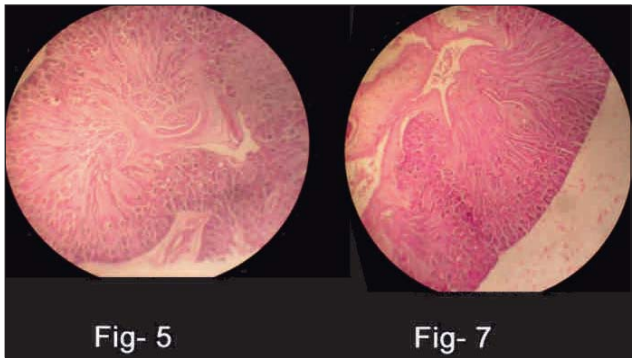

Fig5: Showing cortico medullary differentiation, 18 wks G.A, H&E, 10X10.
Fig 7: Showing well defined pyramidal system, 24wks G.A, H&E, 10x10.

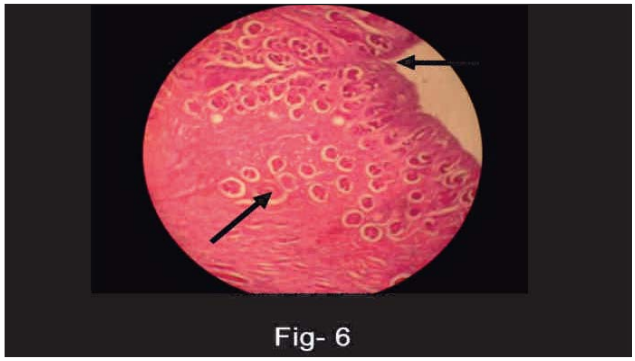

Fig 6: Showing larger deeper glomeruli, 22wks G.A, H&E, 10X40.

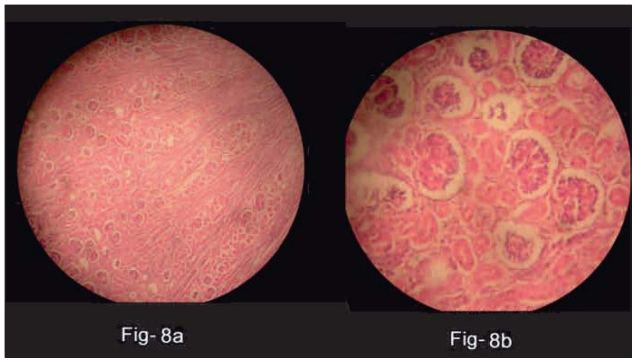

Fig 8a: Showing differentiated pars convoluta& pars radiata of cortex, 34wks G.A, H&E, 10X10.
Fig 8b: Showing pars convoluta in cortex, 34wks G.A, H&E, 10X40.

Fig 9: Showing various stages of glomeruli.

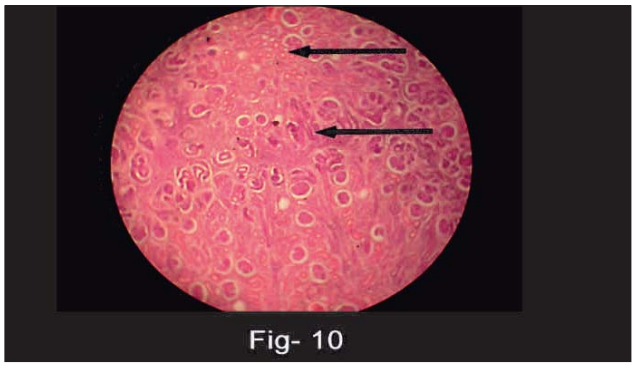

Fig 10: Showing two types of tubules, 16 wks G.A, H&E, 10X10.

Table 1: Showing the number of fetuses in each group

Age	No.of fetuses
A –Group (10-12 weeks)	32
B- Group (13-24 weeks)	11
C – Group (25-40 weeks)	07

Table 2 Showing Mean Length and Mean Width at the Hilum of Both Kidneys of various gestations.

G. A (Wks)	Length of Rt kidney (cm.)	Length of Lt kidney (cm.)	Width of Rt kidney at hilum(cm.)	Width of Lt kidney at hilum(cm.)
10	0.44	0.45	0.18	0.16
11	0.66	0.66	0.15	0.15
12	0.9	0.86	0.17	0.2
13	0.7	0.65	0.1	0.15
14	1.25	1.2	0.2	0.2
15	1	0.93	0.3	0.3

16	1	0.95	0.25	0.35
17	1.35	1.2	0.3	0.35
18	1.4	1.35	0.3	0.4
20	1.54	1.54	0.51	0.51
22	1.9	1.97	0.5	0.5
24	1.88	1.88	0.72	0.68
26	2.05	2	1.6	1.6
28	2.45	2.45	1.9	1.7
32	2.7	2.9	1.8	1.8
36	3.6	3.4	1.9	1.8
40	4.2	4	2.1	2

Table 3 Showing Mean Weights and Mean Volumes of Both Kidneys of various gestations

G. A (Wks)	Mean Weight of right kidney (mg.)	Mean Weight of left kidney (mg.)	Mean Volume of Rt kidney (ml.)	Mean Volume of Lt kidney (ml.)
10	200.8	200	0.25	0.24
11	223.3	225	0.6	0.56
12	247.5	245	0.8	0.8
13	267.5	265.5	0.85	0.85
14	280	285	1.15	1.25
15	320	325	1.66	1.65
16	335	330	1.22	1.2
17	415	410	1.35	1.3
18	465	468	1.45	1.48
20	535	535.5	1.6	1.65
22	1355	1375	1.87	1.92
24	2052	1960	2.62	2.42
26	2575	2570	3.25	3.24
28	3375	3400	3.85	3.95
32	4250	4255	4.2	4.24
36	5100	5200	5.1	5.2
40	5600	5500	6.2	6

ABBREVIATIONS

G.A: Gestational age.

H&E: Haematoxylin and eosin stain.

L.S: Longitudinal section.

PCT: Proximal convoluted tubule.

DCT: Distal convoluted tubule.

Rt: Right kidney.

Lt: Left kidney.

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