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Original Research Article

A study of histological changes during development of human fetal kidney in later half of gestation

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ABSTRACT

Background: Prenatal period is a very crucial time for human development. It is important to know the normal developmental of human kidney for better understanding of various congenital renal conditions.
Methods: This study was conducted in the department of anatomy, Pt. J. N. M. medical college Raipur, Chhattisgarh, India. The materials for study (50 fetuses of gestational age between16 week to 40 weeks from cases of abortions, stillbirth from premature and normal deliveries with apparently normal history of gestation) were obtained from the labour room of the R. N. T. district hospital Kondagaon, Chhattisgarh, India. Fetal kidneys were dissected out; histological slides were made, stained with Hematoxylin and eosin and observed under light microscope.
Results: A Subcapsular nephrogenic zone was seen in all kidneys up to 36 weeks of gestational age. Differentiation of kidney into cortex and medulla was seen in all the specimens. Presence of Bowman's space was seen in 90-95% of glomeruli and vascular pole were present in 65-70% of glomeruli, in all specimens of different gestational age. Parietal epithelial lining of Bowman's capsule was lined by cuboidal epithelium in immature glomeruli but this showed a gradual transition to a flat variety, with the further maturation of the glomeruli. Proportion of glomeruli with many lobulations, went on increasing with increasing gestational age.
Conclusions: From the above findings, it can be concluded that although formation of new glomeruli occurs up to 36 weeks of intrauterine life, differentiation and maturation continues until the last week of third trimester of gestation.

Keywords: Cortex, Human fetal kidney, Gestational age, Glomeruli, Medulla, Nephrogenic zone

INTRODUCTION

Kidney is one of the most important excretory organs of the human body. Prenatal period is a very crucial time for human development. It is important to know the normal developmental of human kidney for better understanding of various fetal kidney diseases. The fetal kidney has about 12 lobes but these are fused in adult to present a smooth surface. The morphogenesis of human kidney begins very early. It assumes a definitive form by the eighth week. Its rudiments are different all along in the pre-natal life and continue to do so even after birth, with the final maturation occurring till 12-14 years of age.[1] The emphasis on genetic counseling and possibility of early prenatal diagnosis has stimulated interest in fetal kidney anatomy.[2]

Definitive human kidney is derived from the mesonephric duct (uretic bud) and metanephric blastema. In brief, the ureteric bud developing from the mesonephric duct dilates and form ampulla. The mesenchymatous tissue

epithelizes and form vesicles which fuse with the ampulla to form a nephron.

Metanephric development begins around 5th week of intra uterine life and terminate in the last month of 3rd trimester of pregnancy with subsequent interstitial growth. Many such nephrons are present in fetal kidney due to multiple branching of the ampullary bud and induction of various mesenchymatous condensates to from nephron arcades. This process of renal development begins at deeper region and reaches the peripheral part of the cortex.[3]

The earlier studies have stressed the histogenesis of the tubules in considerable detail but the glomeruli have not received much attention.[4] It is generally agreed that formation of new nephrons occurs till 34-36 weeks of gestation and the maturation continues up to 12 years.1 Thus at all gestational ages, glomeruli are expected to be in different stages of development, ranging from the most primitive analogue to the full mature type, resembling an adult glomerulus. The detail of this developmental process, still remain to be worked out and are still not clear.

Since there are few reports regarding morphological and histological development human kidney. A Study by Sabita et al5 has stated that the major part of development of fetal kidney occurs during mid-gestation period and continues until the last week of third trimester of gestation. So, the present study was done, to fill the gap of knowledge between the organogenesis and functional maturity of human kidney during pre-natal period. Hence, the aim of current study was to study histological changes during the development of the kidney in later half of gestation.

METHODS

This study was conducted in the department of anatomy, Pt. J. N. M. medical college, Raipur, Chhattisgarh, India. After approval from the institutional ethical committee, the materials for study (fetuses) were obtained from the labour room of the R. N. T. district hospital kondagaon, Chhattisgarh, India. Study was done on 50 fetuses of gestational age ranging from16 week to 40 weeks, taken from cases of abortions and stillbirth, from premature and normal deliveries with apparently normal history of gestation. After the consent of parents, brief antenatal, medical, history from the mother was taken. Fetuses with any external deformity were excluded from the study.

After naked eye examination of fetuses, their crown rump length was measured. Then the kidneys were dissected out. They were immersed and fixed immediately in 10% formalin solution. Entire kidneys were embedded en bloc in paraffin using standard protocol. Tissue block were serially sectioned to generate 5-micron thick section using rotary microtome. The sections after mounting were stained with hematoxylin and eosin and observed under light microscope.

RESULTS

This study was carried out on 50 human fetuses of gestational age ranging from16 week to 40 weeks. Distribution of examined fetuses according to their gestation age, shown in Table 1.

Table 1: Distribution of examined fetuses according to period of gestation.

Period of gestation (weeks)	Number of fetuses
16-24	20
>24-36	23
> 36	07

Histological examination of kidneys was done by using light microscope under 4X, 10X and 40X objective lenses and the following observations were made:

Gross examination

All Fetal kidneys of different gestational ages were found to be lobulated.

Microscopic examination

Subcapsular nephrogenic zone was seen, in all kidneys up to 36 weeks of gestational age (Figure 1). Several developmental stages of the developing nephron were seen in this zone. Below this zone, renal corpuscles of increasing maturity were located at deeper cortical levels. This zone was absent in fetuses of 40 week of gestational age (Figure 2).

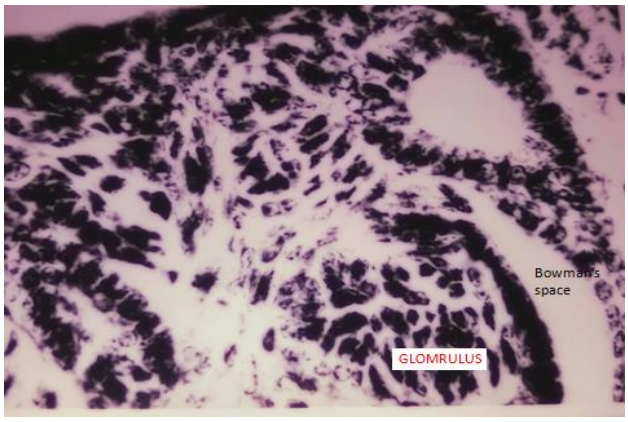

Figure 1: Photomicrograph showing presence of nephrogenic zone (40X. H and E stain).

Differentiation of kidney into cortex and medulla was seen in all the specimens, but in the 16 weeks major part of kidney was occupied by the cortex and a very small part constituted the medulla (Figure 3).

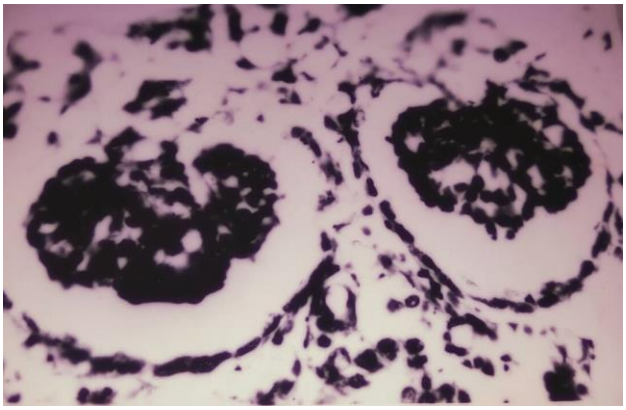

Figure 2: Photomicrograph showing absence of nephrogenic zone in fetus of 40 weeks (40X. H and E stain).

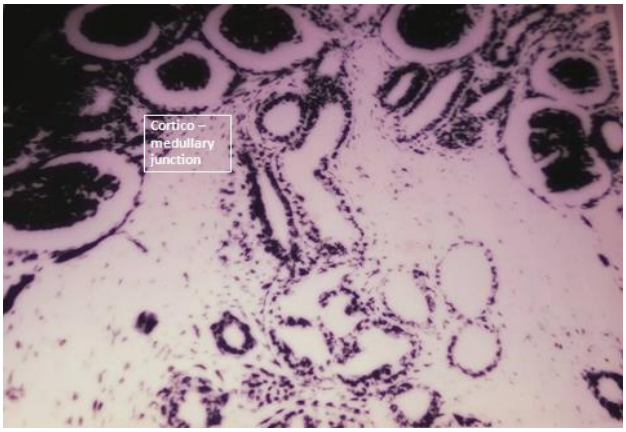

Figure 3: Photomicrograph showing cortico-medullary junction in fetus of 16 weeks (40X. H and E stain).

Glomeruli were seen in different stages of development in the cortex of all the specimens. Most mature glomeruli were found towards the medulla and the primitive analogues were found in the cortex just below the capsule (Figure 4).

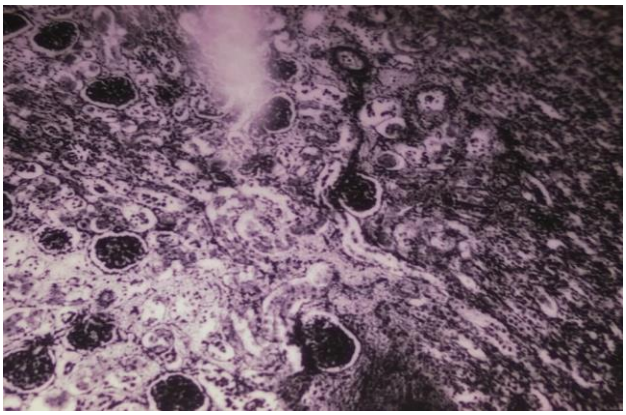

Figure 4: Photomicrograph showing cortico-medullary junction in kidney of fetus of 40 weeks (10 X. H and E stain).

Then 100 glomeruli were studied from each specimen by taking ten glomeruli at random from each section of the specimen, under, high power and oil immersion. Observations regarding the structural characteristics of the glomeruli were made as follow:

Presence of Bowman's space: 90-95% of glomeruli showed the presence of Bowman's Space, in all specimens (Figure 5).

Presence of vascular pole: vascular pole was seen in nearly 65-70% of glomeruli, in all specimens (Figure 5).

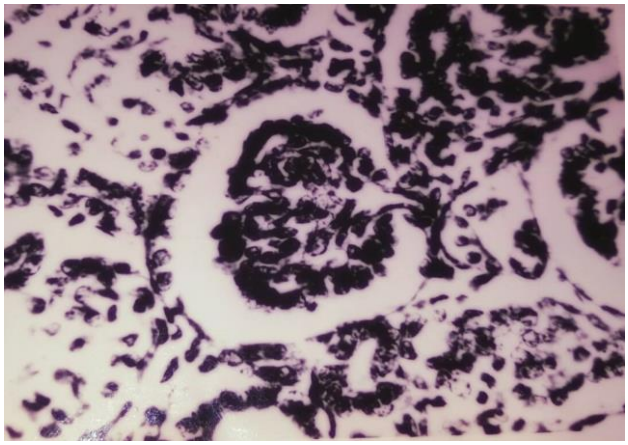

Figure 5: Photomicrograph showing vascular pole and Bowman's space in glomerulus (40X. H and E stain).

Parietal epithelium of the Bowman's capsule: parietal epithelium of Bowman's Space was found to be different in different stages of development of glomeruli. It was lined by cuboidal epithelium in immature glomeruli (Figure 6) but this showed a gradual transition to a flat variety, with the further maturation of the glomeruli. Mixed type (either predominantly flat or predominantly cuboidal) epithelium was seen, depending on the stage of development of the glomerulus (Figure 7 and Figure 8) and completely flat in matures ones (Figure 9).

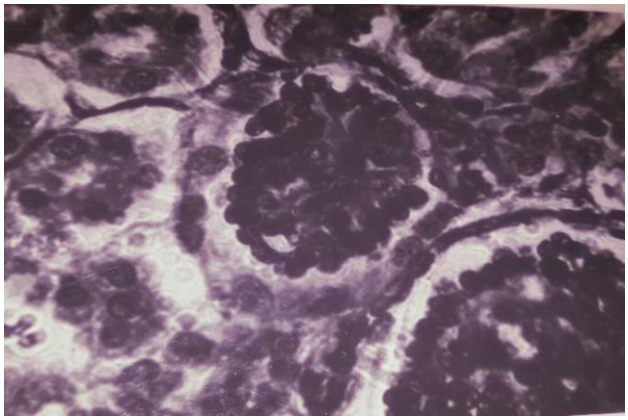

Figure 6: Photomicrograph showing cuboidal epithelial lining of Bowman's space (40X. H and E stain).

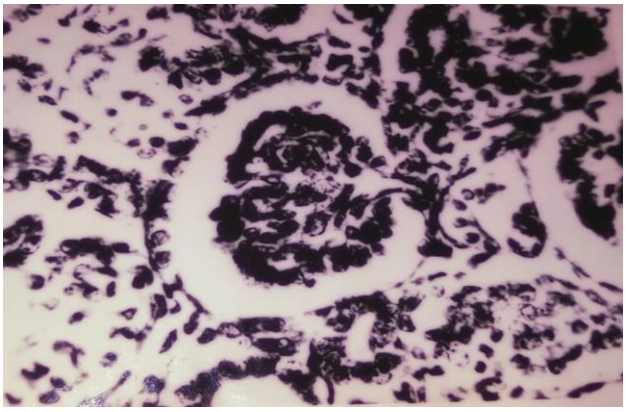

Figure 7: Photomicrograph showing predominantly cuboidal epithelial lining of Bowman's space (40 X. H and E stain).

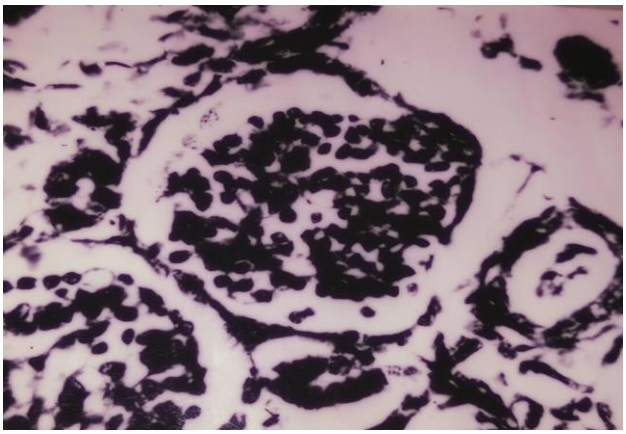

Figure 8: Photomicrograph showing predominantly flat epithelial lining of Bowman's space (40X. H and E stain).

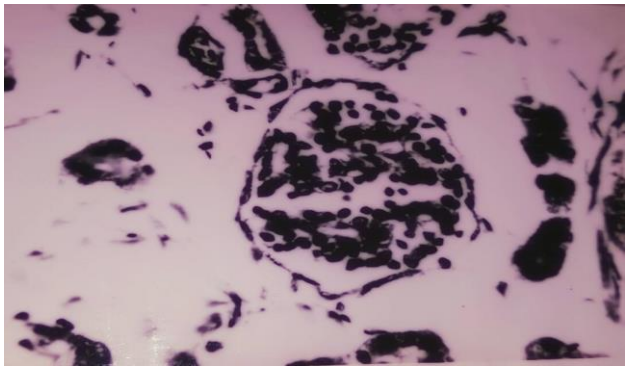

Figure 9: Photomicrograph showing flat epithelial lining of Bowman's space (40X. H and E stain).

The relationship between the epithelial lining of Bowman's capsule and the gestational age (in weeks) is summarized in Table 2.

- At 16 weeks of intrauterine life, 17% of glomeruli were lined with cuboidal epithelium but this number decreased to 7% at 32 weeks, 5% at 36 weeks and finally at 40 weeks only 1%
- At 16 weeks of gestational age, about 75% of glomeruli are lined with a mixed type of epithelium (they were either predominantly flat or predominantly cuboidal). Then there was gradual decrease in the number of glomeruli lined by mixed type of epithelium. This remained 49% at 40 weeks of intrauterine life
- At 16 weeks of intrauterine life only 08% of glomeruli showed a flat type of epithelium, this increased to 50% in 40 weeks of intrauterine life. Thus, mature glomeruli showing a pattern similar to the adult kidney were found to increase in proportion with the increase in gestational age.

Table 2: Epithelial lining of Bowman's capsule in relation to gestational age.

Gestational age	Nature of lining				Total field observed
	Cuboidal epithelium	Mixed type		Flat	
		Predominantly cuboidal	Predominantly flat		
16 weeks	17	30	45	8	100
20 weeks	10	34	39	17	100
24 weeks	11	30	42	17	100
28 weeks	14	19	43	24	100
32 weeks	7	20	43	30	100
36 weeks	5	10	41	44	100
40 weeks	1	8	41	50	100

Lobulations of the glomerulus: according to number of lobulations, glomeruli were graded in three groups.

- Immature glomeruli showing no lobulation: most immature glomeruli did not show any lobulation and a continuous epithelium was seen to surround the endothelial cell mass (Figure 10)
- Immature glomeruli showing few lobulation: glomeruli in subsequent stages of development showed two to four lobules and epithelium was

found either to dip in two to three places or was fragmented (Figure 11)

- Mature glomeruli showing many lobulation: in a more advanced stage of maturation more than 4 lobules were seen and epithelium seemed to have completely disappeared. Thus, glomerulus showed a basic adult pattern (Figure 12).

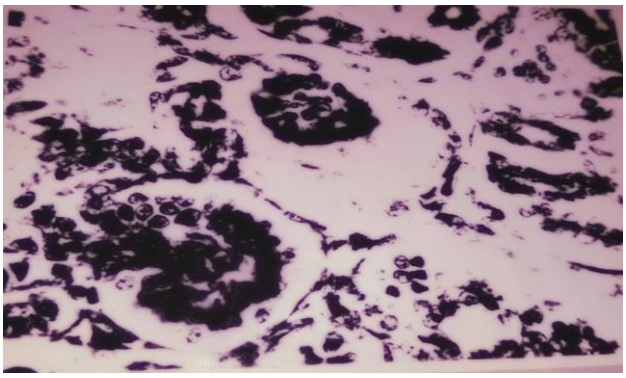

Figure 10: Photomicrograph of immature glomeruli showing no lobulation (40X. H and E stain).

When the above observation was plotted on a Table 3.

- Immature glomeruli with no lobulation showed a decrease from 22% at 16 weeks to 2% at 40 weeks
- Immature glomeruli with few lobulations showed a decrease from 48% at 16 weeks to 34% at 40 weeks
- There was an increase in the proportion of glomeruli showing many lobulation with gestational age. Only 30% of then showed many lobulation in 16 weeks of intrauterine life but this increased to 64% in 40 weeks. Thus, in 40 weeks of intrauterine life 96% of glomeruli showed presence of lobulation and only 2% showed no lobulation. Out of these 96% lobulated glomeruli, 64% resembled a mature glomerulus and 34% were still in initial stages of development.

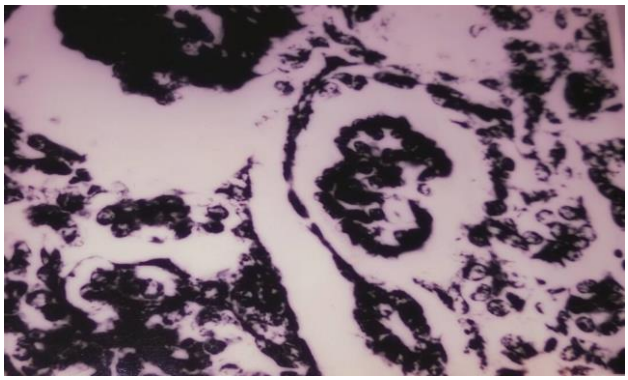

Figure 11: Photomicrograph of immature glomeruli showing few lobulation (40X. H and E stain).

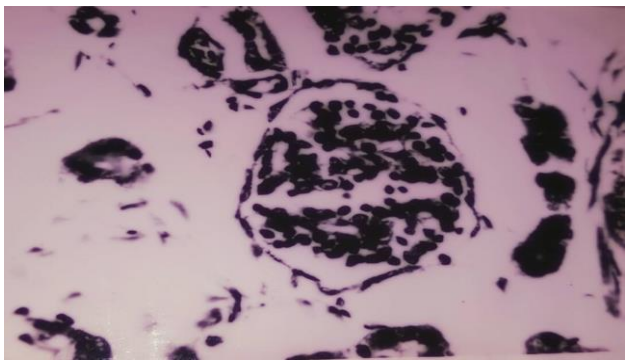

Figure 12: Photomicrograph of mature glomeruli showing many lobulation (40X. H and E stain).

Table 3: Lobulations of the glomerulus in relation to gestational age.

Gestational age	No lobulations	Few lobulations	Many lobulations	Total field observed
16 weeks	22	48	30	100
20 weeks	32	44	24	100
24 weeks	24	46	30	100
28 weeks	20	48	32	100
32 weeks	18	52	30	100
36 weeks	10	45	45	100
40 weeks	2	34	64	100

DISCUSSION

The present study was an attempt towards investigating the structural aspects of the maturation and development of the human fetal kidney in both the qualitative and quantitative perspectives. In current study, all fetal kidneys showed lobulation, irrespective of their gestational ages. Studies by various authors also outlined the presence of lobulation at 14 weeks in utero, while at 16 weeks the kidney fused to from a single organ though the lobulation was still evident.[3,5]

In current study subcapsular nephrogenic zone, responsible for new glomeruli formation was seen up to 36 weeks of pre-natal development. A study by Sadiqali et al, found that 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.[6] Dakovic-Bjelakovic et al, also found that 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.[7] Studies by various authors have mentioned that the nephrogenic zone disappeared at 36th week at 38 weeks and at 40 weeks.[6,8-10] Chikkannaiah et al, observed cessation of neoformation of glomerulus at 35-36 weeks of gestation.[11] In current study, nephrogenic zone was absent in kidneys of fetuses beyond 36 weeks of gestational age, this finding shows that after 36 weeks of intra uterine life, tubules and glomeruli continue maturing, but without the formation of new nephrons.

Various authors have established that the mature glomeruli are located in the deeper cortex near to the medulla whereas the formation of new glomeruli occurs at the periphery of the growing kidney.[7,10,11] Study findings agree with this observation, this indicate that cortex of kidney differentiate from deeper to superficial part.

Present study showed that differentiation of kidney into cortex and medulla occurs before 16 weeks. Some authors found the cortico-medullary differentiation at14 weeks of gestational age and at 18-20 weeks of gestation.[8,12-14]

Bowman's space and vascular pole formed a constant feature in all glomeruli, at all gestational ages, in current study. In the present study, we found vascular pole in two- thirds of glomeruli in all the specimens, of all gestational ages. Osathanondh et al, also found the development of well- defined arcade system (vascular pole) during 18 weeks of gestation.[3]

Some interesting findings of current study was that the nature of parietal epithelium lining of the Bowman's capsules and number of lobulation of glomeruli, were different in different stages of development of the glomerulus, which is still remained unquoted.

Immature glomerulus was lined by a cuboidal epithelium and mature ones showed a flat pavement like epithelium. Glomeruli still developing stage showed a mixed type of epithelium, with a predominance of either cuboidal or flattened type.

It was found that proportion of glomeruli lined with cuboidal epithelium showed gradual decrease, from 17% at 16 weeks to 1% at 40 weeks of intra uterine life. Proportion of glomeruli lined with mixed type of epithelium also showed similar pattern but the proportion of mature glomeruli, lined with flat epithelium increased with increase in gestational age. Thus, at 40 weeks of intra uterine life 50% resembled an adult glomerulus, lined with a flat epithelium, 41% were lined with predominantly flat epithelium.

An immature glomerulus did not show any lobulations but lobulation occurred in the later stage of maturation. Proportion of mature glomeruli (having more than 4 lobules) went on increasing with increasing gestational age. In the 40 weeks of intrauterine life, 64% of glomeruli showed an adult pattern, 2% glomeruli did not show any lobulations and rest showed few lobulations.

The lack of availability of fetuses of first trimester was a limitation of study as it would be possible to explain the developmental process in more detail. Findings of current study may prove useful in defining the fetal kidney diseases such as agenesis, hypoplasia, multicystic kidney, polycystic kidney etc. and help in the diagnosis of fetal age

CONCLUSION

From the above findings, it can be concluded that although formation of new glomeruli occurs up to 36 weeks of intrauterine life, differentiation and maturation continues until the last week of third trimester of gestation to prepare fetus, for transition from fetus to newborn.

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