International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Original Article

A Study on Histogenesis of Human Suprarenal Gland at Various Gestational Age Group: An Observational Study

Sagar M Nerpagar[1], Gautam A Shroff[2], Geetanjali B Sudke[3], Chhaya Diwan[4]

[1]Associate professor; Department of Anatomy, Parbhani Medical College, RP Hospital and research institute, Parbhani
[2]Professor; Department of Anatomy, MGM Medical College and Hospital, Chh.Sambhajinagar
[3]Associate professor; Department of Anatomy; PAH Government Medical College, Baramati.
[4]Professor (Retd.) Department of Anatomy, GMC, Chh.Sambhajinagar.

OPEN ACCESS

Corresponding Author:

Geetanjali B Sudke
Associate professor; Department of Anatomy; PAH Government Medical College, Baramat

Received: 26-01-2026
Accepted: 18-02-2026
Available online: 05-03-2026

ABSTRACT

Background: Microscopically, the adult suprarenal gland is composed of two distinct regions—the cortex and the medulla. The cortex is further subdivided into the zona glomerulosa, zona fasciculata, and zona reticularis. Each of these cortical zones exhibits unique structural characteristics and performs specific functional roles.
Objective: To observe microscopic structure of suprarenal gland at various gestational age group.
Materials and Methodology: The present observational study conducted at Department of Anatomy and Obstetrics and Gynecology of Government Medical College and Hospital, Aurangabad. The study was done on 40 spontaneous abortuses and stillborns ranging from 12th weeks to 36th weeks of gestation. The study was approved by the Ethical Committee of the Institute.
Results: Transitional zone is seen right from 12 week becoming distinct at 22 week and there after gradually decreasing and completely disappearing at full term. At 12 weeks, neuroblastic nodules were seen in the capsule and also in the parenchyma of gland. With increasing gestational age, the number of neuroblastic nodules went on increasing till 22 weeks. After that there is a decline in number of neuroblastic nodule and at 28 weeks neuroblastic nodules were not observed.
Conclusion: The study concludes that, histogenesis of the suprarenal gland demonstrates a progressive increase in gland size with advancing gestational age, accompanied by a gradual increase in capsular thickness and vascularity throughout fetal life.

Keywords: Histogenesis, Suprarenal gland, Stillborn and abortus.

INTRODUCTION

The Anatomy of adrenal gland was described almost 450 years ago in 1563 by Bartholomeo Eustacius and zonation of gland and its distinction from medulla were elucidated shortly thereafter. (1)

Steroid hormones produced by fetal adrenal cortex regulate intrauterine homeostasis, the maturation of fetal organ systems necessary for extra uterine life and in some species the timing of parturition. (Liggins G.C.1976). Appropriate development and function of fetal adrenal cortex therefore are critical for fetal maturation and perinatal survival. (2)

The Development of human fetal adrenal is regulated primarily by adrenocorticotrophin (ACTH) secreted from the fetal pituitary gland. However, as ACTH is not a mitogen per se, its proliferative action on human fetal adrenal cortical cells is thought to be mediated by autocrine/ paracrine growth factors produced by adrenal cortical cells in response to ACTH. In addition, these growth factors appear to modulate the functional response of fetal adrenal cortical cells to ACTH. The role of several growth factors including the Insulin like growth factor I & II (IGF-I & IGF-II), Epidermal growth factor (EGF), Basic fibroblast growth factor (BFGF), Activin, Inhibin and Transforming growth factors alpha and beta (TGF- alpha &

TGF- beta) have been studied. Thus, human adrenal development is primarily regulated by ACTH, but its actions appear to be mediated or modulated by cohort of locally expressed growth factors. The net effect of which results in unique growth and steriodogenic activity of human fetal adrenal cortex. Also, one factor essential for adrenal development is Orphan Nuclear receptor steriodogenic factor (SF-1, AD4BP-NR5A1). [3,4]

The present was conducted to study the histogenesis of fetal adrenal gland at different stages of development in intra uterine life in Marathwada region of Maharashtra.

Objectives:
To observe microscopic structure of suprarenal gland at various gestational age group.

MATERIALS AND METHODS

The present observational study conducted at Department of Anatomy and Obstetrics and Gynecology of Government Medical College and Hospital, Aurangabad. The study was done on 40 spontaneous abortuses and stillborns ranging from 12th weeks to 36th weeks of gestation. Twins and fetuses with gross anomalies were excluded. The study was approved by the Ethical Committee of the Institute.

The gestational age, sex, weight crown-rump length was studied in detail. Weight of fetuses were measured in grams on double pan balance.

The fixation of fetuses was ensured by injecting them with 10 % formalin locally, at various sites with the help of a 10-ml. syringe and 20 number needle in cranial cavity, in the neck and subcutaneously in the upper and lower limbs.
The suprarenal glands were obtained from fetuses by a midline incision over the anterior abdominal wall. Both glands were carefully dissected out, immediately weighed, and initially fixed in 10% formalin. Subsequently, the tissues were cut into small pieces and fixed in Bouin's fluid for 24 hours. Post-fixation, the specimens were dehydrated through graded alcohols—70% alcohol for 6–8 hours, 90% alcohol overnight, followed by three changes of absolute alcohol for one hour each. Clearing was performed in xylene for approximately 30 minutes. The tissues were then infiltrated with paraffin wax at 56–60°C through three changes and embedded using L-shaped moulds. Paraffin blocks were sectioned at 5–7 µm thickness, and ribbons were floated on cold water to remove folds. Sections were mounted on egg albumin–coated slides and dried on a hot plate.

Routine haematoxylin and eosin (H&E) staining was carried out following dewaxing, rehydration, nuclear staining, differentiation, bluing, counterstaining, dehydration, clearing, and mounting with DPX. Selected sections were additionally stained using Masson's trichrome technique to differentiate connective tissue components. The stained slides were examined under a light microscope and photomicrographs were obtained for histological analysis.

OBSERVATIONS AND RESULTS:

In the present study, a total of 40 fetuses (19-males, 21-females) ranging from 12th weeks to 36th weeks of gestation were studied.

Table 1: Showing microscopic structure of Suprarenal Gland across gestational ages:

Gestational Age (Weeks)	Microscopic Findings
12–14	Thin fibro-collagenous capsule with blood vessels. Presence of superficial necroblastic nodules. Definitive cortex seen as a narrow superficial zone of small basophilic cells. Large fetal cortex composed of eosinophilic polyhedral cells arranged in columns peripherally and reticular pattern centrally. Transitional zone present. Neuroblastic nodules and scattered neuroblasts seen. Medulla absent.
15–17	Similar architecture as earlier stage. Capsule vascular. Definitive cortex distinct. Fetal cortex large. Few necroblastic nodules in outer fetal cortex. Scattered neuroblasts present. Increased vascularity with a prominent central vein.
18–20	Dominant fetal cortex with large eosinophilic cells. Peripheral cords and central reticular arrangement with numerous sinusoids. Definitive cortex seen as a narrow basophilic band. Transitional zone prominent with arched cords extending into fetal cortex. Increasing vascularity.
22–24	Capsule well defined and thicker. Definitive cortex, fetal cortex and transitional zone well developed. Transitional zone increases in thickness. Vertical arrangement of cells noted. Neuroblastic nodules decrease. Mild fibrous tissue proliferation observed.
26–28	Definitive cortex increases in thickness. Fetal cortex shows marked degenerative changes with sinusoids, congestion and hemorrhage. Neuroblastic nodules and solitary neuroblasts

	markedly reduced. Chromaffin cells increase, especially near large vessels. Fibrous tissue seen around central vein.
32–34	Definitive cortex organizes into future zona glomerulosa and early zona fasciculata. Definitive cortex invades and replaces degenerating fetal cortex. Sinusoids containing RBCs seen.
35–36	Definitive cortex further thickened, clearly forming zona glomerulosa and zona fasciculata. Increased chromaffin cells near central vessels forming rudimentary medulla.

DISCUSSION

Human fetal growth is a net result of a complex interplay of genetic, hormonal and growth factor effects. Suprarenal gland is essential for intrauterine development of fetus. The fetal adrenal cortex is involved in maintenance of intrauterine homeostasis and in the preparation of fetus for extra uterine life, by regulating the maturation of essential organ systems including lungs, liver and gut.[3]

In the present study, comparison of histological structure of Suprarenal Glands at various stages of fetal life was done with the findings of other workers. It was observed that for definitive cortex of gland, throughout the gestational period definitive or permanent cortex forms narrow sub capsular zone. This finding was corroborative with the findings of Benirschke, Bloch and Hertig [5] (1956). They found that definitive cortex formed 1/5th of adrenal tissue. In present study it was found that definitive cortex is 1/10th at 12 weeks a gestation, 1/8th at 28 weeks of gestation and approximately 1/5th of total cortex at 34-36 weeks of gestation. The cells of definitive cortex are small, polygonal with basophilic cytoplasm and euchromatic nuclei. The findings were similar to that of Bernirschke et al [5] (1956) and Turkel & Itabashi [6] (1974).

In the present study it was observed that the thickness of definitive cortex remains almost the same from 12 weeks to 22 weeks. There after it shows slight increase in thickness up to 28 weeks with a further faster growth. Similarly, according to "Keene & Hewer" that permanent cortex slowly increases in size throughout the intra uterine life. According to Damayanti N. et al [7] (2005), the cytoarchitecture of 12 weeks suprarenal shows a superficial zone and a larger deeper zone. The findings of present study were same as that of Damayanti et al. [7] Uotila [8] (1940) had also mentioned that the cells of definitive cortex did not show any regular arrangement but period of study was only 4-8 weeks of gestation. Bosian-Sobkowska J et al [9] (1993) have found that the zona glomerulosa and outer part of zona fasciculata begin to form by 20th week of gestation. Mesiano & Jaffe [10] (1997) have described that the cells of definitive cortex took the appearance of adult zona glomerulosa by 30 weeks. Damayanti et al[7] had mentioned that from 28 weeks the outer zone of cell organizes into an arcuate shape typical of the future zona glomerulosa.

In the present study it was observed that a larger part of fetal cortex is contributed by fetal cortex. This corroborated with the study of Bernivschke et al [5] (1956) who found that fetal cortex formed 4/5th of adrenal cortex. The cells of fetal cortex were large, polyhydral with eosinophilic cytoplasm and round vesicular nuclei. These findings of present study were similar with findings of Bernirschke, Bluch & Hertig, Turkel & Itabashi and Mesiano & Jaffe. [5,6,10]

In the present study, it was observed that the cells in outer part of fetal cortex were arranged in the form of longitudinal columns separated by capillaries, whereas the cells in inner part were arranged in the form of a network with sinusoidal spaces in between. Because of this arrangement of fetal cortical cells Uotila [8] (1940) described the fetal cortex of suprarenal gland as fasciculo-reticular layer which he found from 7th week onwards. According to Keene M.B & Hewer [11] the fetal cortex degenerated progressively during the last 10 weeks of fetal life, but still contributing to the bulk of the gland till birth.

McNutt and Jones [12] (1970) reported that the transitional zone appeared between permanent and fetal zone by 14th week. Mesiano & Jaffe [10] had described the transitional zone as a zone of finger like columns of cells extending from definitive cortex into the fetal cortex. In the present study also, the transitional zone was seen throughout the studied period that is from 12 weeks to 36 weeks. According to Mesiano & Jaffe [10] by the 30th week of gestation the definitive zone and transitional zone began to take on the appearance of zona glomerulosa and zona fasciculata respectively. In the present study also, it was observed that the zona glomerulosa and zona fasciculata appeared at 34 and 36 weeks.

In the present study these cells were seen scattered throughout the gland and at places, they form groups usually near the large primitive vessels in reticular layer of fetal cortex. This finding was same as that of Antti Hervonen [13] (1971), Turkel & Itabashi [6] (1974) and Bogdanova & Debelenko [14] (1989). These cells were small with round densely staining nuclei surrounded by a thin rim of basophilic cytoplasm. These cells were given different names by different scientists like neuroblasts by Turkel & Itabashi [6] (1974) and Cooper et al [15] (1990)

Phaeochromoblast by RE Coupland [16] (1952), primitive symphathetic cells by Antti Hervonen [13] (1971). A group of these neuroblasts was called a neuroblastic nodule by Turkel & Itabashi [6] (1974). They described that these neuroblastic nodules

were avascular and non-capsulated but they lie in contact with capillaries and fetal cortical cells. The appearance of neuroblastic nodules in the present study was similar to that found by Turkel & Itabashi. [6] However, Antti Hervonen [13] (1971) reported that these primitive symphathetic cell groups were avascular and partly capsulated.

In present study at 12th week, neuroblastic nodules were seen invading the capsule of the gland and also the parenchyma. Solitary neuroblasts were also seen scattered throughout the gland. With increasing gestational age, the number of neuroblastic nodules increased reaching maximum at 22 weeks showing decline thereafter. They were absent at 34 and 36 weeks. These finding are corroborative with the study of Turkel & Itabashi [6] (1974) but they had found that the maximum number of neuroblastic nodules were observed between 17-20 weeks of gestation. However, other workers including Keene & Hewer [11] (1927) and R.E. Coupland [16] (1965) had reported that after 30 weeks neuroblastic nodules slowly regressed so that few nodules remained by the time of birth.

In the present study solitary neuroblasts were observed from 12 weeks to 28 weeks of gestation, the number decreasing thereafter with very few neuroblasts being present at 36th week. Antti Hervonen [13] (1971) and Turkel & Itabashi [6] (1974) had reported similar findings. But according to Cooper et al (1990) neuroblasts were absent after 28 weeks of gestation. Decrease in neuroblastic cell number in later fetal period was because of their conversion into other cells. According to R.E. Coupland [16] (1952) these neuroblasts were converted into chromaffin cells from 8th week onwards.

According to Antti Hervonen [13] (1971) neuroblasts in peripheral part of the gland were converted into chromoffin cells whereas neuroblasts in the central region of nodule differentiated into sympathetic ganglionic cells from 11th weeks onwards.

Turkel & Itabashi [6] (1974) had reported that the decline in neuroblastic nodules was due to the differentiation into chromaffin cells by apoptosis of neuroblasts.

In the present study it was observed that the number of neuroblastic nodules goes on increasing, but with the conversion of neuroblasts into chromoffin cells, nodules & solitary neuroblasts both decreased and chromaffin cells increased. These chromaffin cells have slightly basophilic cytoplasm with round nuclei, peripherally condensed chromatin and were intermediate in size between that of neuroblasts and fetal cortical cells. R.E. Coopland [16] (1952) and Antti Hervonen [13] (1971) have described the chromaffin cells similar to this.

In the present study, few chromaffin cells were seen at 22 weeks. The number of these chromaffin cells gradually increased upto 36 weeks forming the rudimentary medulla. Chromaffin cell were found at same stage of gestation i.e. 22 weeks by Keene & Hewer [11] (1927). Chromaffin cells were found at an earlier stage than the present study by R.E. Coupland[16] (1952) and Antti Hervonen [13] (1971), who found chromafin cells 8 weeks on wards and 11 weeks onwards respectively. Mesiano & Jaffe [10] (1997) had found few chromaffin cells at 30 weeks i.e. at a later stage than the present study.

In the present study rudimentary medulla was found at 34-36 weeks, whereas Bogdanova, Debelenko [14] (1989) and Cooper et al [15] (1990) had reported the presence of rudimentary medulla at 30th week. Similarly, Mesiano & Jaffe [10] (1997) observed that medulla was absent at birth and rudimentary medulla was formed around central vein in the first postnatal week which became adult like by 12-18 months.
Capsule is seen at 12th week of gestation which is very thin. The thickness of the capsule increases by deposition of collagen fibers as the gestational age advances. Vascularity of the gland is found to be increased throughout the gestational period studied i.e. 12 weeks to 36weeks**.**

CONCLUSION

The study concludes that, histogenesis of the suprarenal gland demonstrates a progressive increase in gland size with advancing gestational age, accompanied by a gradual increase in capsular thickness and vascularity throughout fetal life. Histologically, the gland is organized into three distinct cortical zones—definitive zone, transitional zone, and fetal zone—whose relative proportions change with maturation. The definitive cortex constitutes approximately one-tenth of the total cortex between 12 and 20 weeks of gestation, increases to about one-eighth by 28 weeks, and further expands to nearly one-fifth by 36 weeks, reflecting progressive cortical differentiation and replacement of the fetal zone.

REFERENCES

1. Cope CL. The adrenal cortex in internal medicine. I. British Medical Journal. 1966 Oct 8; 2(5518):847.
2. Ishimoto H, Jaffe RB. Development and function of the human fetal adrenal cortex: a key component in the fetoplacental unit. Endocr Rev. 2011 Jun;32(3):317-55.
3. Sangma GTN, Ibochoucha Y, Damayanthi N. Development and Maturation of suprarenal glands in human fetuses .J.Anat.Soci.India 2008;57(1):1-7
4. Ram KS, Sharma M, Sharma A.Histogenesis of suprarenal gland in fetuses of different gestationa age groups. Int .J.Biol Res.2013; 4(1)2675-2682.

5. Benirschke K, Bloch E, Hertig AT. Concerning the function of the fetal zone of the human adrenal gland. *Endocrinology*. 1956;58:598–625.
6. Turkel SB, Itabashi HH. The natural history of neuroblastic cells in the fetal adrenal gland. *Am J Pathol*. 1974;76:183–203.
7. Moore KL, Persaud TVN. *The Developing Human: Clinically Oriented Embryology*. 7th ed. Philadelphia: Saunders; 2003. p. 303–304.
8. Uotila UU. Embryological development of fetal and permanent adrenal cortex in man. *Anat Rec*. 1940;76:183–203.
9. Bocian-Sobkowska J, et al. Cytological aspects of human adrenal cortex development during intrauterine life. *Folia Morphol (Warsz)*. 1993.
10. Mesiano S, Jaffe RB. Developmental and functional biology of the primate fetal adrenal cortex. *Endocr Rev*. 1997;18(3):378–403.
11. Keene MFL, Hewer EE. The development of the human suprarenal gland. *J Anat*. 1927;61:302–324.
12. McNutt NS, Jones AL. Ultrastructural observations on cytodifferentiation in the human fetal adrenal cortex. *Lab Invest*. 1970;22:513–527.
13. Hervonen A. Fine structure of paraganglia and adrenal medulla. *Acta Physiol Scand*. 1971;83(Suppl 368):46–94.
14. Bogdanova TI, Debelenko LV. Ultrastructure of human adrenal glands at various periods of prenatal morphogenesis. *Arkh Anat Gistol Embriol*. 1989;96(4):69–76.
15. Cooper G, Hutchins GM, Israel MS. Histogenesis of the human adrenal medulla. *Am J Pathol*. 1990;86:357–370.
16. Coupland RE. The prenatal development of the abdominal paraaortic bodies in man. *J Anat*. 1952;86:357–370.
17. Barbet JP, Bargy F. Development and regression of the fetal adrenal cortex. *Bull Assoc Anat (Nancy)*. 1987;71(212):37–44